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CHRONIC EPIDEMIC
ENCEPHALITIS

*Contributions from
The Psychiatric University Laboratory and from The Clinic
for Nervous and Mental Diseases of Copenhagen*

CHRONIC EPIDEMIC ENCEPHALITIS

BY *e*
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WITH PREFACE BY
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PREFACE

By Sir *Fredk. W. Mott*, M. D., F. R. S.

DR. WIMMER was kind enough to send me the advance sheets of his valuable monograph on Chronic Epidemic Encephalitis, with a request that I should write a short Preface to his work. I esteem it an honour to do so, for I feel that he has conferred a great boon on the English-speaking medical profession in discussing fully from his own extensive experience and study a subject which is now of great importance to medical men, and is likely to become still more so, having regard to the fact that recently there has been in England a great increase in the number of cases notified of Lethargica Encephalitis. Thus the Ministry of Health has given the number of cases notified for the first five months of the year as 2,473, the annual average for the whole period of the past four years being 839. A considerable proportion of these cases must pass into the chronic stage, and they will fall into different types according to the location of the pathological process in the central nervous system, the common form having the Parkinsonian syndrome.

That the subject is of great importance is shown by the fact that quite recently the Ministry of Health has issued a Memorandum on Encephalitis Lethargica, and has specially directed attention to the value of local enquiry as to the presence of mild abortive or unrecognised cases. As Dr. Wimmer points out in his very valuable monograph, epidemics seem to vary as regards the proportion of cases which develop a chronic form. Moreover, as Netter said, Encephalitis may remain several months, several years. The virus remains then living in the nervous centres like that of Syphilis. Seeing that it «may remain active for years within the central nervous system as an intermittent or recurrent process, which, however, in by far the majority of cases is of a progressive nature» — it follows that mild abortive or unrecognised cases may subsequently develop serious symptoms. The whole of this question is discussed in a masterly manner in this monograph.

The recently issued memorandum by the Ministry of Health points out that from the clinical point of view there are three types distinguishable, (1) general disturbance of the functions of the central nervous system without localisation, (2) various localisations in the central nervous system, and (3) mild or so-called abortive cases. Dr. Wimmer deals with the chronic forms, and evidently he accepts Netter's view that the virus may still remain active, therefore the various forms of Chronic Encephalitis Lethargica can hardly

be regarded as sequelae, as the Memorandum indicates, but as effects on the nervous system of a still active virus. At present all we know about the virus is that it is a filterable virus, and that its location is the naso-pharynx. Numbers of experiments on animals have been performed, and doubtless more light will be thrown upon this extremely interesting disease, which probably has existed for centuries past — as is pointed out in the Memorandum above mentioned — but only recently have we come to recognise it as a definite diagnosable infective disease.

I feel convinced that this book will be of great service at the present time on account of the lucid, scientific and practical manner in which the subject of Chronic Epidemic Encephalitis is discussed by Professor Wimmer. The author has not only had a large experience of this disease, but has studied it from the pathological as well as the clinical side, and made himself familiar with the extensive current literature, especially with the important contributions of French and German Authorities.

Frederik W. Mott.

AUTHOR'S PREFACE

The balance of epidemic (lethargic) encephalitis has not yet been struck: Besides the deaths resulting directly from acute or subacute cases of this disease, the number of which amounted, in some epidemics, to forty percent (v. Economo), we still meet with ever increasing numbers of "remnants", chronic, delayed, frequently very severe and invalidating nervous affections which are due to the persistence, within the nervous system, of the virus of epidemic encephalitis.

Thus, the acute febrile, maybe lethargic, stage very often represents only the "up-beat" to a chronic disease, the onset of which may, in other cases, be quite insidious.

Chronic epidemic encephalitis constitutes a new chapter of Neuropathology, a "chapitre d'attente", as H. Claude puts it, seeing, that even if we have already learnt a good deal about it, we still, in time to come, may expect to be confronted with new clinical pictures of this most protean disease, by French neurologists so justly termed "une maladie à surprises et à reprises".

In presenting, in this book, my personal experiences on chronic epidemic encephalitis, I do not pretend to give the final description of this polymorphous disease. I only hope that my monograph may be of some use to my colleagues

in the diagnosis of these nervous troubles, the true nature of which is sometimes very difficult to ascertain.

The cases of chronic epidemic encephalitis revealing the symptomatological pictures of "parkinsonism" or "hyperkinesias" have already become rather well-known to medical men. In my book, I have, to some length, insisted upon a group of "intermediary types", of a somewhat different symptomatology. I feel convinced that in time to come, such cases will prove to call for our most accurate diagnostic judgement.

Sir FREDK. W. MOTT has judged my book worthy of a preface by his hand. All medical men know what that means to a book. Here, I only want to give expression to my gratitude and, still more, to my feelings of admiration for the high scientific works of a master of English Neuropathology.

As a young man, I worked for half a year in the National Hospital for The Paralysed and Epileptic, Queens Square, where I had the great privilege of being initiated in the English Neuropathology by Sir VICTOR HORSLEY and Dr. BEEVOR; and I should like, in submitting this monograph to the English-speaking medical profession, to have it regarded, too, as a modest tribute to the memory of these prominent and renowned investigators of neuropathology and the physiology of the nervous system.

I want to thank my co-workers in my hospital, especially my chief assistant of the Psychiatric University Laboratory, Dr. Axel V. Neel, the original papers of which, upon epidemic encephalitis, will be found amply quoted in the following pages.

The reader will easily perceive that I have drawn largely upon the excellent foreign literature on epidemic enceph-

phalitis. I should think, however, that, for various reasons, I am mostly indebted to French neurological literature upon this matter, in the first place to the numerous and original papers from the Clinic of Professeur PIERRE MARIE, and the Department of M. SOUQUES, at the Salpêtrière

Finally, I have to thank THE RASK-ØRSTED FOUNDATION for contributing to the publishing of my book.

Copenhagen, June 1924.

AUGUST WIMMER.

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L'encéphalite peut durer bien davantage, plusieurs mois, plusieurs années *Le virus reste donc vivant dans les centres nerveux*, comme celui de la syphilis.

NETTER.

INTRODUCTION.

Not very long after the extensive outbreaks of epidemic ("lethargic") encephalitis it was noticed that, following the acute phase of the disease, a series of nervous disturbances, often extremely tenacious and deleterious, would frequently persist. While, at first, there was a tendency to consider these nervous cases as "sequels", reliqua, following on an acute but in itself abated inflammatory affection of the central nervous system, numerous experiences gained during later years have forced the view upon us that the encephalitic process may remain active for years within the central nervous system as an intermittent or recurrent process which, however, in by far the majority of cases, is of a progressive nature. Furthermore, the experiences obtained with regard to these chronic, epidemic cases of encephalitis — which have been sadly numerous — soon taught us that the cases may be, and often are, of a chronic and insidious nature from the very beginning; thus, the early history of a case very often fails to show the acute "classic" infectious phase, with its characteristic triad of symptoms: fever, lethargy, eye symptoms (or other mesencephalic signs). In such cases the clinician very often has to face extreme difficulties of differential diagnosis.

When v. Economo in 1919 recorded a case of „chronischer, schubweise verlaufender Encephalitis lethargica”

(with autopsy), he said: "Gewiss ist diese chronische Verlaufsform im Bilde der Encephalitis lethargica bisher ein Ausnahmefall." Experience, however, soon showed that the frequency of these "chronic forms" was terribly high, highest perhaps after the more recent epidemics (Naville, Stern). It is impossible at present to establish the percentage of frequency in proportion to that of the acute, cured forms. But, it is evident from the records of numerous observers that the absolute frequency is quite considerable:

In 1922 Souques reports 102 cases, two thirds of which presented "parkinsonism". Subsequent to 1919 Catola (of Florence) observed 27 such cases. Of Moris Grossmann's 92 patients, 62 showed more or less progressive nerve symptoms. Price finds chronic, nervous "sequels" in 43 % of his encephalitic cases. W. House has 55 chronic forms among 145 cases. Holthausen & Hofmann report 62 cases of this nature. v. Economo (1923) considers that about two thirds of the cases which survive the acute phase, pass into a chronic stage. According to Sicard (1923) this happens in more than half of the cases. In Geneva, Naville finds among 200 cases of encephalitis 46 with "sequelles", "parkinsonism" being the predominating syndrome; Bing & Stachelin, too, have 36 cases of "parkinsonism" out of 97 encephalitic cases; Reys 39 out of 94 and, besides, 31 cases with other forms of "sequels". Adler (Prague) records 51 chronic forms out of 77 cases. F. Stern, among 107 patients, found 59 with a "chronic-amyostatic syndrome"¹⁾. Moreover, Mlle Lévy of Pierre Marie's department at the Salpêtrière has quite recently, in an extensive study based on a material of 129 cases, described the "manifestations tardives" of epidemic encephalitis.

¹⁾ In a later compilation of 203 cases Stern finds about 70 % with chronic progressive development (Remarks in the discussion following the communications on encephalitis at the meeting held in Vienna in April 1923 by "Deutsche Gesellschaft f. interne Medizin").

To these cases must be added those which had already been reported by Netter, Redalié, Cruchet, Pierre Marie & Mlle Lévy, H. Claude, Babinski, Meige, Mourgue, Trétiakoff & Bremer, Bériel, Sicard & Paraf, Géronne, Hunt, Morris-Allen, Boyd, Oeckinghaus, Fuchs, Gerstmann & Schilder, E. Schultze, Pette, Moewes, Nonne, Hess, Stertz, Speidel, Späth, König, Haushalter, Girardi, Mingazzini, Meggendorfer, Français & Lhermitte, Marinesco, Schaller & Oliver, and others. In Denmark cases have been described by V. Christiansen, Levison, Gulstad, Holst, in Norway by Zeiner-Henriksen, in Finland by Hagelstam, Ehrnroth, in Sweden by Antoni, Wiggert, and others.

As opposed to this great frequency of nervous cases it is of some interest to emphasize the strikingly rare occurrence of non-nervous affections, such as pulmonary, cardiac, renal or anæmic affections, as sequels to epidemic encephalitis (Naville). The "neurotropism" of the encephalitis virus seems to be still more pronounced than, for instance, that of the influenza virus.

As has already been mentioned, the acute febrile (in certain cases "lethargic") initial phase is often absent in these chronic forms of encephalitis, or the initial stage is more or less vague. This fact is emphasized by several of the above mentioned authors, most recently by Mlle Lévy. In 38 out of his 59 chronic cases Stern finds, however, an initial "Kopfgrippe", or acute encephalitis. Among my own patients it was only in a minority of cases that I was able to obtain information which indicated a fairly typical "encephalitis lethargica". Far more frequently there was an indication of a short, common, febrile phase, without the encephalitic triad, and which was designated by the physician in charge of the patient, or by the patient himself, sometimes as "influenza", sometimes as "the Spanish disease" (commonly called "the 'flu"). And, as far as a considerable number of my patients are concerned, the initial phase of the infection seems to have passed partially or absolutely unnoticed, apyretically, or, at any rate, with so little fever that the case has been

one of "ambulatory encephalitis". Or, again, there is no previous history of a febrile phase, and we have to deal with one of those "cryptogenetic" cases of chronic encephalitis which cause the very greatest diagnostic difficulties (see, for instance, Cases 7 and 34). Wallgreen, of Sweden, among 190 workmen, of whom only one had had a marked epidemic encephalitis, found 59 more, who showed some signs of a chronic encephalitic condition, viz. spasms, tremor, diplopia, dyssomnia, asthenia, headache, and the like¹).

In some few of my cases there are records of two or more (even up to five, Case 37) attacks of "influenza" or "Spanish disease" prior to the onset of the chronic nervous affection. These attacks of fever are mostly mild and of short duration²), the interval between them ranging from a couple of months to several years. Should, now, the first attack be regarded as a true influenza preparing the soil for the encephalitic disease, as it has already been suggested by v. Economo? Or should this and the following attacks be considered as febrile encephalitic relapses, corresponding to the hyperthermic phases sometimes encountered in the course of a chronic encephalitis (Ledoux, Lhermitte, Stern, Gulstad; cf. my own observations)? Or, could it possibly be a matter of reinfection, such as, as, for instance, our Cases 19 and 36 might suggest? An attempt at answering these questions will be made later on (Pathogenesis p. 302).

Judging both from the casuistics and from my own personal experiences it seems to be of little or no consequence in regard to the form, degree, and rate of development of a chronic epidemic encephalitis, whether there has been a strongly pronounced, may be "lethargic" initial phase or not. An uninterrupted chronological clinical connection between the acute initial stage and the chronic nervous affection, is by no means necessary; it is, per-

¹) Svenska Läkaratidn. 1921; p. 18.

²) In one of my cases (complicated parkinsonism, Case 26) there was a lethargic relapse, quite as serious and of longer duration than during the first fever attack.

haps, found most frequently in the cases of "parkinsonism" (for instance 25 times in Bing & Staehelin's 36 cases), at any rate in so far as rigidity is concerned, while the tremor, if it does occur at all, usually sets in later; but, in cases of parkinsonism, and more especially in the other forms of encephalitis, there is often an interval, wholly or partially free from nervous symptoms, permitting the patient to resume his work, undergo his military service (Renaud; also one of my own cases), etc. —

The length of the interval varies considerably, from a couple of months to two, three, or four years (Netter, Catola, Meggendorfer, Naville, Stern, Price, Nonne, Mlle Lévy, Guillaume & Gardin, Mc Alpine, and others), variations which will also be found in my own reports.

According to Barré & Reys, changes in the spinal fluid should persist during the intervals, anyhow during the first eight months; however, this does not correspond for instance with the experiences of Stern, nor quite with those of our own department (cf. page 216). Nor is this assumption necessary for the understanding of the chronicity or recrudescence, respectively, of the process: the virus can, no doubt, be "latent" within the nervous system itself (cf. p. 300).

But, whether there is an interval or not, whether this interval be free from neurologic (or humoral) changes or not, the most characteristic feature of the chronic forms of epidemic encephalitis is in almost all cases the persistent progressiveness, at any rate as far as the general clinical picture is concerned: already existing symptoms increase in intensity and extent, or the clinical picture eventually assumes the appearance of a gradually intermerging mosaic of variegated nervous symptoms, sometimes slowly progressive, sometimes of a more acute or subacute course of development, now indicating an increase in the morbid process within the already affected area of the central nervous system, and then indicating that other, more remote areas have become affected; etc.

Notwithstanding that the disease is undoubtedly chronic, the individual symptoms nevertheless often reveal themselves in attacks, just as there may also occur, for a time at any rate, more or less marked regressions. The causes of the relapses (which are sometimes accompanied by fever, Cases 39 and 36) usually remain undiscovered. For the present we can only parallelize with the conditions in other chronic infectious diseases, such as syphilis, disseminated sclerosis, etc. A rather interesting fact, which has been emphasized by E. Meyer, and more especially by Mlle Lévy, is that the exacerbations of the disease in women are not unfrequently found to coincide with gravidity (in 17 out of Mlle Lévy's 77 cases), a coincidence which is also known from chorea gravidarum, and, in a less pronounced degree, from disseminated sclerosis ¹⁾.

The general clinical picture of chronic epidemic encephalitis, then, is that of a nervous disease, principally of a progressive and chronic character, but frequently phasic in its further development, the individual symptoms distinctly indicating — by their nature and the character of their onset — the disseminated localisation of the morbid process within the central nervous system, with a pronounced predilection for certain definite areas of the same (the extrapyramidal system, cf. below). Therefore, one of the chief characteristics of chronic encephalitis is a considerable symptomatological polymorphism, a pronounced “*plasticité symptomatique*” (Lhermitte), a variability in respect of both the grouping of the symptoms and their mode of development, which is by no means inferior to the clinical pictures of nervous diseases due to syphilis or to that of disseminated sclerosis, and which is amply illustrated in many of my own cases ²⁾.

¹⁾ Some authors (Lemierre, Roger) point out the incidence of exacerbations with the winter season (“seasonal exacerbations”; compare Fig. 11).

²⁾ Especially polymorphous cases have been reported by Jaquin, Canteloube, and others.

SYMPTOMATOLOGY.

Naville observes, in his comprehensive survey on "sequels" to lethargic encephalitis, that the nervous symptoms in these chronic forms of encephalitis "are less numerous and less varied than would be expected". — This remark seems a little surprising and may doubtless be attributed to the special peculiarities of those patients who came under his personal observation. For, otherwise, the symptomatological polymorphism (of course not always found in one single patient) is constantly emphasized by most authors, as has already been mentioned. There can be no doubt that some of the symptoms belonging to the acute phase — frequently the ocular symptoms, for instance — may disappear wholly or partially where the affection is, or will become, chronic. But, on the other hand, other symptoms occur, more especially certain "extrapyramidal", myatrophic symptoms, etc., which are not present, or at any rate only slightly indicated, during the acute phase.

The fundamental feature of the symptomatology of chronic encephalitis¹⁾ is, no doubt, at any rate in a very large number of cases, the extrapyramidal syndrome in its various forms (as will be described later). However, this syndrome is in itself on the one hand extremely varying in its aspects, while, on the other hand, it very rarely

¹⁾ The description of the clinical picture of acute epidemic encephalitis is outside the scope of the present work; readers may be referred to the well-known monographs: v. Economo: *Die Encephalitis lethargica*. Wien 1911; Achard: *L'encéphalite léthargique*. Paris 1921; Tilney & Howe: *Epidemic Encephalitis*. New York 1920; Stern: *Die epidemische Encephalitis*. Berlin 1922.

happens that it is not blended with symptoms from other areas of the nervous system — a fact which is borne out also by the experiences from my own department —, thus rendering the general clinical picture extremely protean.

It appears as if the encephalitis virus can invade and occupy, as it were, any area of the nervous system and cause pathological changes, a fact which would readily explain the symptomatological polymorphism. Between the two extreme limits of the extrapyramidal syndrome, the almost purely akinetic-dystonic syndrome (parkinsonism), and the hyperkinetic syndrome, ranges a rather numerous group of intermediary types, possessing more or less pronounced components from the extrapyramidal syndrome and, in addition, and more especially, presenting other nerve symptoms such as affections of the cranial nerves, pupillary disturbances, bulbar symptoms or pyramidal signs, muscular atrophies, general nervous troubles, psychotic, vegetative or endocrinal symptoms, etc. etc.

In order to make this survey more lucid, an attempt will be made to classify into main groups those cases in which the neurological symptoms are predominant. Prior to this, however, a survey of a series of more general symptoms or syndromes, with which the purely neurological type is often interwoven, will be given.

PSYCHOTIC AND GENERAL NERVOUS DISTURBANCES.

True psychotic symptoms, especially those appearing as sharply defined psychotic phases (confusion, delirium, agitation, etc.), belong chiefly to the acute (febrile) initial stage of encephalitis; they may, however, occur also at a later stage of development of chronic encephalitis (cf. Cases 7, 45, 46, 59, 61), most frequently

perhaps as a more transitory state of blurred consciousness followed by amnesia and, perhaps, combined with neurological signs of a paroxysmal character (cf. Case 28)¹).

More persistent psychotic disturbances encountered during the course of chronic encephalitis have been described by Hesnard, Holthusen & Hofmann, Hess, Kisby & Davis, Auden, Patterson & Spence, Bremer, Staehelin, Diemitsch & Schilder, Runge, Kirschbaum, Hübner, Kauders, Westphal, Stern, Briand, G. Petit, Truelle, Mlle Lévy, Logre, Robin, Laignel-Lavastine, and others. The observations made in our department have recently been recorded by Kn. Winther²).

In adults we sometimes find emotional disturbances, depression, hypochondriacal ideas, sometimes connected with obsessions (H. Claude), or impulsions, under episodic dysphoria (Kirschbaum). Expansive emotional disorder is much less frequent, and usually confined to a somewhat inane euphoria. The depression may develop to a high degree, and may, for instance, lead to attempts at suicide (cf. Case 5 and 45) or even to suicide itself (Claude, Petit, Staehelin).

It may be that these psychotic "sequels" of epidemic encephalitis will, in time to come, prove rather frequent. For, during the last year, I have seen in my wards quite a number of "atypical" psychoses, in young and aged people, in which there was found a previous history of "Spanish disease", or the like, from which the patient had not fully recovered, suffering from fatigue, emotional erethism, anxiety, dyssomnia, increasing depression, hallucinations of sight or hearing, most frequently hypnagogic, etc. Slight rises of temperature were very often observed, or, again, fine myoclonic jerks in

¹) In the patient mentioned as Case 26, I found nocturnal, later also diurnal, visual or auditory hallucinations (accusations of being a syphilitic), followed by reactions of despair etc., a stage of hallucinatory confusion.

²) Ugeskrift f. Læger 1923, p. 73 (Danish).

the limbs. One patient developed a marked adiposity and some slight indication of parkinsonism; etc.

These observations will be dealt with more fully in a later publication, as will also be a series of cases in which the psychotic symptoms have more or less preceded the neurological ones (Case 2, 42), a phenomenon to which attention has been drawn by G. Petit.

According to what I have seen of these emotional disorders, the type is essentially different from that found in the maniacal depressive psychosis. It is of course not altogether impossible that a latent disposition may sometimes be mobilised by the encephalitic infection. But, as a rule, the true maniacal depressive elements, the true inhibition, the characteristic flight of ideas, are absent in emotional disorders of encephalitic origin. The desolate condition of the patient often seems conspicuously to indicate a psychogenic origin of the depression. Evidence of this may be found in Case 5. The emotional disorder of this patient was however soon lost in the main psychotic picture which most frequently occurs in chronic encephalitis, especially in parkinsonism, often being in existence from the very onset of the disease, namely the *bradyphrenia* (Naville)¹). Like other encephalitic mental affections the *bradyphrenia*, too, may reveal certain "oscillations" (G. Petit); but, as a rule, it is inclined to be monotonously persistent, and, as far as we are able to judge at present, it is frequently progressive. According to Naville, the *bradyphrenia* is "surtout caractérisée par une diminution de l'attention volontaire, de l'intérêt spontané, de l'initiative, de la capacité d'effort et de travail, avec fatigabilité objective et subjective et légère diminution de la mémoire". In many respects this mental dulness recalls the purely motor sluggishness found in parkinsonism, the *bradykinesia* (see p. 35). Naville characterises it in one place as "une sorte de somnolence ou de léthargie chronique":

¹) L'Encéphale 1922, p. 369 and 423.

“Dans les formes sévères de cette déchéance, les malades semblent mener une vie exclusivement végétative; ils sont complètement inertes et sans activité psychomotrice, et sont même incapables de s’habiller seuls et de manifester les désirs les plus élémentaires; leur extrême lenteur d’idéation et de mouvement, leur paresse affective et leur impassibilité pathologique trouvent leur expression dans l’altération et l’immobilité du visage”.

From a purely symptomatological point of view there is here an interweaving of a psychic and a physical “viscosity” (Verger & Hesnard); possibly some of the symptoms of bradyphrenia may be accounted for by primary motor disturbances (Naville and others; cf. p. 316); the specific psychic nature of bradyphrenia has not by any means yet been elucidated; we only know with certainty that we have first and foremost to deal with an inhibition, and not, or only in a slight degree, with true mental defects¹). Furthermore, in the case of encephalitic parkinsonism, as in the classic paralysis agitans, we should be strictly on our guard not to be deceived by the character of “apathy”, “emotional stupor”, “lack of initiative” etc., which the purely motor rigidity gives to the entire mentality and behaviour of these patients; compare also my cases.

The same holds true as regards the mistaking of these cases for dementia præcox. Foreign authors, especially French (Laignel-Lavastine, Logre, Dide, Guiraud & Lafaye, Claude, Kahn, and others), record cases resembling dementia præcox subsequent to encephalitis. The diagnosis of these cases, however, would appear to be far from reliable; “catatonic” symptoms alone are not sufficient ground for making the diagnosis; and, taken as a whole,

¹) One of my patients (Case 26) complained that she found difficulty in translating her thoughts into words, she was more slow of thought, her attention was more rapidly fatigued, but above all, she felt it to be a trouble that she had lost interest in her surroundings, and that she could not “feel” as before”.

the resemblance found between these types of cases seems to be of an extrinsic semiological character only ("apparence de démence précoce", Deny & Klippel¹⁾; compare later on p. 214.

More or less marked disorders of memory may appear in encephalitis as in other infectious diseases, affecting either the faculty of reproduction or of retention, sometimes giving rise to an amnesic syndrome, for instance a pseudo-Korsakov (Hesnard, K. Winther, and others). At the time of writing I have in my department a man, 28 years of age, who in 1915 and 1917 had protracted febrile attacks (without reliable lethargic or mesencephalic symptoms) and who in 1923 began to suffer from a noticeable weakening of the faculty for retaining newly received impressions. There were no other psychotic symptoms. The most minute neurological investigation showed nothing abnormal. In the spinal fluid, however, 68/3 cells were found, chiefly small lymphocytes, some few larger mononuclear ones, globulins 1, albumins 20¹⁾; the Bordet-Wassermann reaction in serum and spinal fluid was negative. Suspicion of chronic encephalitis is in this case highly justifiable, and a further close observation of the patient is required.

In my Cases 51 and 55 we have circumscribed loss of memory with ambulatory automatism. In my Case 17 the patient showed memory disturbances of a very peculiar kind.

While in the ward, he already experienced difficulty in orientating himself topographically; for instance, he would always forget whether he had his clothing in the right or in the left wardrobe, etc.

When he returned home, he could not recognise his home, "everything seemed strangely altered, as if quite new to him"; even a photograph of himself he could scarcely recognise. In the streets he will often pass

¹⁾ Revue neurologique 1922 p. 402.

¹⁾ As to the meaning of these figures compare later p.

by old friends, not recognising them until he hears their voices. When walking in the streets, he feels quite as if he were walking in a foreign town. The streets and houses, previously well known to him, look thoroughly unfamiliar; he has to be very attentive, and to scrutinise the boards with the names of the streets, lest he lose his way. When leaving his house, he does not know what direction to take to get to the Hospital, which is quite close to his home. When, after his illness, he first saw the "Round Tower" of Copenhagen, he did not recognise it, nor could he think of its name until some time afterwards. He remembers the names of the streets, of his acquaintances, etc., but completely fails to "localise" them, when needed. People and surroundings do not look "inhuman" or "hideous" to him. There is no emotional apathy; no true involvement of intellect except for a mild impairment of immediate memory, and a difficulty of collecting varied simultaneous impressions, as, for instance, in newspaper reading or when conversing with people.

In children and very young individuals changes of morals and character are the features which principally stamp the picture, frequently revealing a curious uniformity in different patients.

These disturbances seem to be sadly frequent: of 25 children suffering from encephalitis epidemica, treated in 1918—1922 at the Hospital for Epidemic Diseases in Copenhagen, 11 died; 2 could not be traced afterwards; the remaining 12, who survived, all displayed psychic disturbances, to a more or less pronounced degree (K. Winther).

The psychic disturbances may occasionally occur during the initial stage of the disease (Case 1); in most cases, however, they set in at a later period, having a slow development. The fully developed cases are sometimes reminiscent of "erethic imbecility" (Bonhoeffer), sometimes of certain hypomaniacal, unproductive states of excitement: restlessness, garrulousness, meddlesomeness, wide awake yet erratic attention, curiosity, moods of

foolish mirthfulness, irritability; queer manners (case 2 a); desire to tease, querulousness, marked emotional irritability with uncontrolled outbursts of anger, scolding, and the use of abusive language, propensity to destructiveness, biting nails, automutilations (Case 14), smearing about with fæces and urine, wilful spitting or micturition on surrounding persons or objects (Mlle Lévy, Staehelin), violence, attempts at murder (Briand, Staehelin, Sherman & Beverly), attempts at setting fire to hospital beds (Mlle Lévy), cruelty towards children or animals (Sherman & Beverly, Briand & Rebould-Lachaux, Staehelin), truancy from school, vagrancy, begging (Staehelin), dishonesty, mendacity, denunciations (Robin, Staehelin), pilfering (Case 6), pilfering at the stores (Tinel), sharking, a mythomantic component being often unmistakable (Case 61). A great trouble in many of these child-cases is a precocious (paradoxical) erotism, sometimes combined with a somatic pubertas præcox (Fig. 15, Case 14), leading to masturbation, obscene language and conduct, exhibitionism (Mlle Lévy), attempts upon adult females, or offences towards small girls (Case 1); the chronic encephalitis thus already begins to assert itself in forensic psychiatry; and these children will no doubt in the future create a lot of trouble to the Public Institutions for the care of difficult children¹).

At school, owing to their lack of concentration, their unreliable faculty of perception and retention of ideas, their failing interest in their work, and perhaps primarily on account of their lack of mental perseverance, these children become backward.

The psychic disturbances in children and young individuals described above may be complicated by bradyphrenia (Cases 6, 13), a combination which, however, so far as my experience goes, is not very frequent. According to Dr. Kn. Winther's systematic investigation of our

¹) In these children, also, we occasionally encounter attempts at suicide during emotional outbursts or during "dreamy states" (Staehelin).

material it is doubtful whether actual defects of intellect are present in the majority of cases. It is, however, possible that other conditions will be found in quite young children (Patterson & Spence, Hofstedt, Hübner, and others).

It is interesting to note that these psychotic disturbances in children may show the same "nocturnal type" as is found, for instance, in certain respiratory disturbances attending encephalitis (p. 68): During daytime the child may be perfectly, or almost perfectly, normal, but towards evening at a regular fixed hour it may develop a condition of violent restlessness, chattering, singing, desire for motion, visual hallucinations, etc. Pfaundler, Hopp & Blackfan, Fletcher, Findley, Patterson & Spence, Briand & Borel, Mlle Lévy mention such "nocturnal" exacerbations" ¹⁾.

In adults, as well as in children, the psychotic symptoms are usually paralleled by the more or less pronounced and persistent neurological, general nervous, vegetative symptoms, more especially by disturbances of sleep of various kinds, respiratory troubles, etc.

The following observation, Case 1, is of some interest in this connection. As has been mentioned, the first psychotic attack follows closely upon the initial lethargic phase. Then follows a period of remission, lasting some time, after which a fresh outburst of neurologic symptoms (hemimyoclonia resp. hemichorea) and, some time later, serious deterioration of character, an erotism leading to criminal acts.

Case 1. Boy, 14 years old, son of a mechanic; no previous nervous attacks; mental powers normal; lively, good, docile boy.

At the beginning of August 1920 typical encephalitis lethargica ²⁾: fever, somolence, deliria, ptosis, diplopia, paresis n. facialis dext. In about 3 weeks' time after onset rather marked failing

¹⁾ In our Case 14 there are, transitorily, hypnagogic visions.

²⁾ The boy had been engaged at an office together with a boy whose father had died from "sleeping sickness" two months before.

of faculty of retaining newly-received impressions. In September more pronounced psychic changes: he began singing, shouting, all day long, became unreasonable, used abusive and impolite language, swore, became violent, destroyed things, struck his fellow patients, etc.

He was admitted to my department 17th September 1920, extremely unmanageable, fought, kicked, bit, used very abusive language, spat out his food, voided in his bed, showed himself unwilling and contrary during examination, shouting "shut up" and "idiot", etc., to the examining physician.

He was perfectly clear of mind and able to orientate. There was no persistent emotional disorder, such as true manical exaltation; nor flight of thought or productivity. His "naughtiness" often bore the mark of (reactive) attacks, with intervals of relative tranquillity, on certain days with a state of light somnolence.

He could be rather malicious, for instance coaxing the nurse to come up to his bed and then striking her face with his fist. Or he threw excrements at those around him, spat like a lama, tried to bite, etc. etc.

Masturbation was not observed; but he seemed to be rather impressed by a female student, patted her cheek, wanted to kiss her and called her "a sweet girl".

At nights he was often sleepless, would sing out and scold, etc.

At a clinical demonstration, during which he listened to our description of his various merits without seeming the least impressed, he alleged that he was not able to remember much about them, he believed we intended to beat him, when we came near his bed. He knew what season it was, but said he could not tell the month or year, nor the name of the hospital. His whole behaviour, however, seemed somewhat feigned, almost as though he was acting a part.

Neurological findings: normal reaction of the pupils, no certain paresis of eye-muscles or facial muscles. Positive Babinski reflex, ankle-clonus, and highly exaggerated patellar reflex on the left side; only slight weakening of power in left arm and leg; no hemi-rigidity, neither tremor nor involuntary muscular movements. No trace of parkinsonism.

Temperature normal throughout his stay at the hospital. No albumin, nor sugar, in the urine. Hæmoglobin 80 %. In the third week of illness spinal puncture showed: cells 21/3, globulins 2, albumins 20.

His erethism gradually abated, and on his discharge from the hospital on 27th October 1920, he was a rather decent, normally lively boy, without any morbid moods. Systematic

tests of his intellectual powers (Dr. Kn. Winther) showed that these were normal for his age.

April 6, 1922, he was again admitted. For about one year he had been able to attend work as a mechanic's assistant. During this period he began to suffer from choreatic jerks in left arm and leg, headache, vertigo, attacks of excessive perspiration; from November 2nd to December 5th, 1921, he was at Bispebjerg Hospital. Here he revealed a troublesome erotism, showed indecent attention towards the female staff, constantly hanging about the nurses. He was extremely agile and garrulous. He was discharged, but, at his home, his erotism again manifested itself; he could not let small girls alone in the street, shouted obscene language at them, etc., so that he got a bad reputation in the district.

On readmission to our department he was rather quiet, somewhat infantile, and showed some regret at his conduct. No definite emotional reactions; perhaps he was rather a little too self-satisfied and unconcerned. His general behaviour was good, perhaps a little too "attentive" towards the nurses. Systematic tests of intellect showed no visible defects.

Height 158 cm; weight kgs. 40,300. General habitus rather childish; penis and scrotum, however, well developed; vigorous growth of pubes, no growth of hair in axils nor on upper lip. Infantile voice.

In left arm and leg, and occasionally in left half of face, he had mild choreiform jerks, sometimes more myocloniform twitches. No apparent hemiparesis; no clonus, nor Babinski reflex. On the whole, the neurological examination showed no further abnormalities. Spinal puncture: cells 2/3, globulins 0, albumins 10. Negative Bordet-Wassermann reaction in serum and spinal fluid. He was discharged after a few weeks' stay at the hospital.

After discharge he has been extremely unmanageable at home, obstinate, teasing, cannot get on with those around him, behaves badly in the street, scolds people, pushes them or trips them up, pushes their parcels from them, etc. He teases a younger brother, threatens him with a spanking, likewise threatens his mother when she blames him, but afterwards he collapses, weeps, and is penitent. His affection for his family has waned considerably.

Physically, his body is constantly restless, he "writhes", "wriggles" with his arms, head and body; he constantly and heedlessly belches and spits, often on people in the street. Always restless, cannot sit quietly on a chair for five minutes at a time, extremely troublesome with his requests, extremely

inquisitive, meddlesome, always interfering in conversations, "impossible to keep him silent", cheeky, chattering, childish in his remarks and perceptions; according to the mother's judgment almost as childish as the younger brother of nine years. Frequently he shows absence of mind, "as if he was walking in another world", may pass his parents in the street without noticing them; no vagrancy; no definite signs of hallucinations. General humour changing, usually, however, "impassive", singing, whistling; the confinement, for instance (cf. below), he took very quietly.

He has become "a very slovenly and uncleanly boy"; his mother must scold him in order to make him wash himself, change clothes, etc. But he is not uncleanly with urine and stools.

He goes to sleep at night, but after about an hour's slumber he will often talk in his sleep, shout out, in most cases alluding to events which have happened in the day; sometimes he gets out of his bed, eyes open, but does not react when spoken to; he does not seem to feel any anxiety. Never enuresis, nor fits.

His erotic tendencies, however, cause the greatest trouble: He constantly follows small girls, his small cousins included, clumsily obtrudes and "clings" to adult females, or uses foul language. The parents have not observed masturbation, nor do they think he has had intercourse with adult women.

He was admitted once more on the 28th May 1923, this time sent in by the Court for observation: May 11th, he had been arrested for misdemeanour towards small girls of from 6 to 12 years; evidently he had misbehaved in this respect numerous times in the course of a year, or more; in most cases he had lured the child into a gateway, or the like, had manipulated her abdomen or genitals, according to his own assertion always outside the child's clothing, and had exhibited his own genitals to the child. At the trial he said that the desire to commit this offence came suddenly upon him, always attended by erection, never by ejaculation. He asserts that he has not had sexual intercourse with adult women, nor attempted actual coitus with the children. He has had a propensity to masturbation.

Psychically his main condition is almost the same as during his last stay at the hospital: he twaddles childishly, chatters, constantly asks to be removed to another department, etc. He seems bashful when spoken to about his misdemeanours, otherwise he is in high spirits and unconcerned, participating with liveliness in the life of the department, in-

quisitory and meddlesome to the point of cheekiness: only reluctantly and after repeated admonition does he conform to the rules of order in the department; some days' confinement to bed has a good influence upon him in this respect. Occasionally he quarrels with his fellow-patients. He constantly runs after members of the female staff without however having committed actual assaults upon any one of them.

No true exaltation, no flight of thought or ideatory productivity; no defects of intellect; no schizophrenic traits.

Physical examination shows on the whole the same conditions as during previous stay: height now 163 cm, weight kgs. 48,700. General appearance hardly more virile. No neurologic symptoms of any kind whatever now.

Case 2. In another youth of 20 years the predominating symptom was vagrancy. Having previously been normal psychologically, following upon an encephalitic attack at the age of 15, he became dull, lazy, constantly sleepy, began to disappear from home, a day at a time; once, however, a fortnight; he sauntered idly through the streets, usually ending by sitting down somewhere and going to sleep. He himself stated he suddenly felt a desire to wander, in a few cases provoked by his mother's remarks, but generally without any such exogenic dysphoria. He only had a vague recollection of his wanderings. There were never epileptic attacks.

He was admitted to this department the first time in 1919, before I was in office; the diagnosis was then supposed to be that of a dementia praecox, and he was removed to St. Hans Hospital (Lunatic Asylum at Roskilde). After two years he was discharged, but again brought to my department in September 1923, by the police, because he had threatened his mother with a knife during a quarrel at home. His psychic condition on the whole seemed to be unchanged; he was indolent, slept much, and constantly attempted to escape from home. He had become more loutish, intriguing, teasing, etc. He had, nevertheless, been able to work as an apprentice for about a year.

As before, he gave an indolent impression; systematic testing of the intellect revealed no apparent defects. There were no traits of schizophrenia either in his process of thinking, conduct, or in his moods. He was an orthoregulator¹⁾. The humoral syndrome was normal.

There were no demonstrable neurologic symptoms during his first stay here, nor at the lunatic asylum. Not until his second admittance, 5 years subsequent to the onset of the

¹⁾ Compare below p. 30.

illness, did such symptoms appear: Rather pronounced Babinski reflex on the left side, slight ankle-clonus on the left, patellar clonus on the right side. Right arm is occasionally pronated by quick, non rhythmical, myoclonic jerks. No pareses, nor hypertonia, no static, nor action tremor, no pronounced bradykinesia. No ocular pareses, normal eye grounds, pupils reacting well to light and on accommodation, but there is a marked tendency to anisocoria, as sometimes one, sometimes the other, pupil becomes the larger in diameter. The oculopupillary reflex is not especially pronounced (reduction of pulse rate 8—12).

We rarely find such coarse moral deterioration of character in adults as in youths and children. If we meet it occasionally, it usually denotes a premorbid, psychopathic personality (Jones & Raphael).

General nervous disorders of a somewhat different kind are however frequently found, dominating the picture for a long period, and, as it was also sometimes in the cases with true psychotic symptoms, correlative, objective neurologic morbid signs are not always present.

The patients often complain of a sensation of fatigue, up to maximum asthenia, manifesting itself both as rapid exhaustion during work, and as a decreased rate of working; coincident with this there is often a painful feeling of incapacity or "indifference" towards the daily work. When there is parkinsonism this symptom is often extremely pronounced, emphasized as it is by muscular rigidity; in one of my patients it became so violent that he was compelled to lie down very frequently.

This phenomenon is possibly of an endotoxic (endocrinal?) origin, and reminds one of the asthenia found in "l'insuffisance surrénale" (Sergent). v. Sarbo has described typical myasthenic phenomena in cases of chronic encephalitis, and it is a well-known fact that the connection between myasthenia and endocrinal disturbances has been the subject of much discussion during recent years.

In other cases the patients are troubled with headaches, either persistent or paroxysmal, attended by drowsiness, yawning, etc. (Case 20) or, as in Case 55, by a sympathetic, oculopupillary syndrome. Sometimes there are marked congestions of blood in the head; or, we have swoons, fits of vertigo, etc. (Cases 18, 20, etc.).

Sometimes also we find a conspicuous emotional erethism: excessive sensitiveness with outbursts of weeping, the patient being easily scared, fits of anxiety, reactive or endogeneous, quick temper, fits of anger or rage, etc. Usually the patient has a painful recognition of the fact that his emotional equilibrium is easily disturbed.

Taken altogether, conditions which remind one of "psychasthenia", "neurasthenia", or which have a more or less "hysteriform" aspect, the correct diagnosis of which is possible only by a thorough investigation into the etiological factors and a minute search for concomitant symptoms of a certain organic nature (neurologic, vegetative, etc.).

DISORDERS OF SLEEP.

An extremely persistent and painful symptom in chronic encephalitis, in children as well as in adults, is insomnia; the French speak directly of "*une forme insomnique*".

Sometimes we have cases of almost complete insomnia, where the patient lies wide awake all through the night. In other cases there is dyssomnia, either in the form of difficulty in falling asleep, or a constantly interrupted sleep, attributable to bodily pains, myoclonic unrest, and, in patients with parkinsonism, to general restlessness caused by difficulties in assuming a comfortable position. In other cases, again, the patient is constantly awakened by attacks of fear, terrifying dreams, etc.

In some cases, we have pronounced attacks of pavor nocturnus and, more especially in children, other forms of nocturnal excitement with various types of muscular restlessness ("jactatio nocturna")¹; myoclonic, choreatic, grimacing unrest; snorting, coughing, noisy respiration; grinding of teeth, talking in sleep, tossing violently about in the bed or on the floor, tearing the bedclothes, etc., (Case 14). Or, we have true somnambulism, with more or less complicated acts (Cases 1, 21, 24, 55); or "dreamy states" (onirisme nocturne), the latter more especially in children (Briand; cf. above p. 15).

This inversion of the biological rhythm², which we know also from other organic cerebral affections (senile, paralytic, etc.), is often still further emphasized by the fact that those patients who are sleepless at night show a very marked drowsiness in the daytime, either persistently (as in Cases 6, 13), or in attacks, manifesting itself in diurnal somnolence (Cases 15, 21, 33) of various types during which various neurological symptoms may occur (Case 28).

Case 2 a. A slightly feeble-minded boy of 8 years, who is for the present time in my department, has from his earliest days showed nocturnal motor unrest, turning about in his bed, tossing his head from one side to the other, etc. Subsequent to a severe encephalitic, febrile phase in 1920 he developed strong myoclonic and choreic movements. His nocturnal unrest, too, now became much worse, strong choreic tossing of arm and legs, grimacing movements of face also occurring during night, and, what should be especially noted, he now manifested the same motor unrest when going to sleep during daytime, a fact that had not been observed by the mother before his encephalitis. He was not

¹) Mlle Levy, and other authors, too, state that previously existing neurological symptoms, for instance muscular unrest, have a certain tendency to "recur" in the night (or in the evening).

²) According to Mendicini's investigations (Revue neur. 1920 p. 778), the respiratory rhythm of encephalitic patients during daytime is identical with that of normal individuals during sleep.

awakened by even strong motor unrest during his sleep. Sometimes there was some somniloquia, never noctambulisme.

He has always had a tendency to nocturnal enuresis. Subsequent to his encephalitis, however, he developed a most pronounced polyuria, having to void urine "every other minute" during daytime, and, though the mother would awake him three or four times in the night that he should void his bladder, still she frequently would find him in the morning, "swimming in urine". In the day although he went to bed at 7 o'clock in the evening, he was very drowsy and would most surely go to sleep whenever his mother left him to himself.

During the two first years of his present illness he had been completely mute, not being able to utter anything but a "uhm" or the like, whereas, according to the mother, his word intelligence was thoroughly spared. When, gradually, recovering his speech, he spoke quite correctly, not in the babbling way of a child learning to speak, a fact which impressed the mother very much. Some few months ago, he developed a rather peculiar way of eating, picking the food from the plate with his lips, "like a hen" (he always took great interest in fowls), and he often, especially when left alone, would cackle or crow. In the same period, he would frequently tell the mother that people were "flowers", mostly tulips, being unable, however, to give other particulars of these illusions.

In the ward the above-mentioned nocturnal motor unrest has been observed. He shows a most striking "solemn" gait, rather bradybasic and broadbased, and there is a marked hyper-tonia of the legs and a slight trace of Babinski sign. Some rare myoclonic jerks are seen now and again in the fingers, the toes, the thighs. There are no pareses, no ocular symptoms, no disturbances of speech. In the spinal fluid is found $1/3$ cells, 0 globulins, 9 albumins, the Wassermann reaction being negative in spinal fluid and the blood.

VEGETATIVE, SYMPATHETIC, "ENDOCRINAL"
SYMPTOMS; "DYSREGULATIO AMMONIACA";
CACHEXIA.

Symptoms of the above-named nature are of frequent occurrence in chronic epidemic encephalitis, sometimes singly, sometimes in groups.

Thus, in parkinsonism, we have mentioned the frequently occurring salivation. In this case, as in the classic paralysis agitans, it may of course be attributable to immobility on the part of the entire oropharynx, difficulty in swallowing, etc. In one of my patients, for example, the salivation only occurred when he was lying down. A primary hypersecretion from the salivary gland itself cannot, however, be wholly disregarded. According to Netter, and others, the salivary glands often harbour the encephalitis virus; swelling of the parotid gland is mentioned by several French authors; the syndrome of Miculicz, for instance, by Guillain, Kudelski & Lieuteaud; and, moreover, in a case of chronic encephalitis, Marinresco demonstrated by an autopsy histo-pathological changes in the salivary glands. An analogy with these disorders may be found in the excessive flow of tears described in one case by Claude & Dupuy-Dutemps¹).

Other patients, for instance those with parkinsonism, myoclonias, etc., frequently suffer from fits of perspiration, either general or localised. Of very frequent occurrence — if not absolutely pathognomonic of the encephalitic parkinsonism — is the so-called “greasy face”, (by the French called “visage huileux”), first described by Toby Cohn (“Salbengesicht”), consisting in a marked glossiness of the skin of the face which, together with the amimia of the patient, gives a strange effect.

True edemæ, cutaneous hæmorrhages, or herpetic eruptions, are rarely found, a fact which is of some interest. Babonneix & Pegniaud have described a peculiar affection of the tip of the fingers²). Bed-sores belong to the final cachectic stage of the disease.

¹) Revue neur. 1921. p. 716.

²) Revue neur. 1923 p. 402. In the Neurological Society of Copenhagen I demonstrated in 1920 a male case of 65 years in whom a strio-pallidal syndrome had developed, (hemirigidity, hemitremor), which could not definitely be referred to any previous infection, and who during the last 8 years has suffered from acrocyanosis and a nail-disease (onychogryphosis) in both hands.

Vasomotor disturbances and functional cardiac disturbances are very frequent; these I have often noted myself. Many patients complain of congestions, occasionally accompanied by giddiness; during the lethargic attacks distinct changes of colour in the face are frequently observed; the patient mentioned as Case 8 had sudden attacks of pallor of the face, sometimes lasting as long as half an hour (without, however, any loss of consciousness, and without noticeable changes in the rate or strength of the pulse). Several other localised vasomotor disturbances have been described: rash, peripheral cyanosis and coldness, dermographism, etc. H. Claude, Laignel-Lavastine, and others, insist upon the frequency of such vasomotor sympathetic symptoms. In Case 55 we have a pronounced sympathetic oculo-pupillary syndrome¹). In many cases, too, the oculocardiac reflex is found to be exaggerated (Laignel-Lavastine, Kennedy, Davis & Hyslop, H. Bouttier²)).

Some few authors (Barré & Reys, F. Stern, Mlle Lévy, Bing) state that they have found, in a number of cases, more or less pronounced arterial hypotension; in by far the majority of my own cases the blood pressure was found to be within the normal limits. Like other investigators I often found functional cardiac disorders. Sometimes bradycardia, as in Cases 28, 45, 31, but far more often tachycardia, which may attain considerable dimensions and become very persistent, and to which I am inclined to attach a certain diagnostic value.

Tachycardia may run parallel with an increase in temperature, as in Case 41; in this patient, however, it persists after the temperature has become normal, thus showing its independence of the hyperthermia. In other

¹) Cadwalader describes a sympathetic ophthalmoplegia, miosis, contracted palpebral fissure, mild retraction of the eyeball (Jour. Amer. med. ass. 1921, LXXVII. 121).

²) Rev. neur. 1920. p. 753. Compare the pupillary dilatation provoked by compression of the gangl. cervicale supr. in Case 55.

cases the increase in temperature is very slight, but the tachycardia very marked (Case 47); or, there is absolute absence of hyperthermia (Cases 4 og 7). In several of these cases the tachycardia persisted throughout the attack; in other cases it occurred in phases; for instance in Case 32. Then, again, in Case 8 an initial tachycardia gradually subsided into a bradycardia.

It cannot be said to be proved that the tachycardia always has its origin in the central nervous system; we cannot disregard the possibility of finer pathologico-anatomical changes, for instance, in the nervous apparatus of the heart itself.

Dr. H. Bing, Physician in chief of the medical department at the Municipal Hospital, has most kindly subjected some of my patients who showed a persistent or episodic tachycardia (among others the Cases 7, 8, 13, 25, 32, 46, and 47) to a very thorough stethoscopic examination; X-raying of the heart and electrocardiograms were also taken.

In Case 25, slight increase of pulse tension was found, and accentuation of 2nd aortic tone; in corroboration of these findings the electrocardiogram indicated a mild hypertrophia of the left ventricle. In Cases 13 and 47, normal conditions of the heart were found throughout. In Case 32 there was a slight systolic murmur, otherwise nothing abnormal; neither in Case 7, 8, or 46.

In some few cases pronounced subjective cardiac symptoms are met with, viz. palpitations, dyspnea, precordial pains, etc., sometimes occurring in paroxysms (Reys). Thus, the patient in my Case 45 had several cardiac paroxysms, accompanied by cyanosis or strong pallor of the face, the pulse during the attacks becoming very low, soft, slightly irregular, now and again almost imperceptible. The attacks would last for two minutes at most. Usually the consciousness was slightly clouded; once or twice she became quite unconscious. Apart from a slight presystolic murmur no conclusive objective signs of an organic heart disease could be found on a close examination.

Anæmia is of rare occurrence in chronic epidemic encephalitis; it seems, at any rate, to belong preeminently to the terminal cachectic stage.

Blood tests have been carried out by Stern in 34 cases. Frequently he found the total leucocyte count increased, up to 19000 cells, and above; there were also variations in the numbers of lymphocytes, eosinophil cells, etc. On the whole, the results were extremely variable, and did not show any relation for instance to the clinical findings of the cases (relapses, fever, etc.). Therefore, at present, it would be premature to draw any definite conclusions from the blood tests in regard to the possible existence, in the blood, of toxic substances, or the like.

It is only rarely that we find albuminuria, or other signs of renal affection, in chronic encephalitis. The same may be said of reliable signs of hepatic affection. Occasionally this was seen in some of my own cases — for instance a mild urobilinuria was found; icterus seems of rare occurrence (except in the cases of Barré & Reys). Obvious hepatic symptoms, thus, do not enter as components in chronic encephalitis. Whether certain changes do, however, take place in the functions of the liver, will be dealt with in another section ("pathogenesis", p. 296).

Attention has long been focussed on the frequent metabolic changes manifested in the general state of nutrition of the patients.

Many of these patients show a striking tendency to grow excessively fat (H. Meige, Livet, Netter, Nobécourt, Mlle Lévy, v. Economo, Westphal, and others). In several of my cases this feature is also well-marked, for example in Cases 4, 9, 13, and 41; in the last mentioned case the patient put on 25 kg in weight in a couple of years¹). This adiposity is found not only in the rigid state of parkinsonism, but also, as seen especially in Case 41,

¹) In a patient, mentioned p. 328, the basal metabolisme was reduced by 30 %; she put on 27 kgs. in 6 weeks.

in patients with myoclonia, etc. The adiposity is general, rarely segmental or lipomatous; in a girl of 15, I saw a voluminous and isolated hypertrophy of the mammae. The adiposity has not the character of true adiposalgia. It may be a more transitory symptom, as in one of my young patients with parkinsonism. The possible endocrinal origin of this phenomenon will be referred to later (cf. "pathophysiological mechanisms").

Independent of this adiposity, there are other symptoms suggestive of "dyscrinia": polyuria is not infrequent of occurrence, with or without pollakuria (Briand & Ruquier, Gosset & Gutmann, Bernard (diuresis of 20 litres), Hoke, Bychowsky, Stiefler, Thone, and others). In our Case 55, the diuresis amounted to 12—13 litres during daytime, whereas, during the night, there was no micturition. Coincidentally, some patients suffer from a more or less pronounced polydipsia. Usually this only denotes the presence of a diabetes insipidus; in rare cases, however, there is a true glycosuria (v. Economo, Groebbels, Guillain & Gardin, Higier, and others), which is generally only transitory, as was also the case in a few of my patients (Cases 3, 4, 5, 8, 30, 39), and rarely found at a later stage of the encephalitis (Claude).

An adiposo-genital syndrome has been described by Maranon, Potet¹⁾, Barkman²⁾, Stiefler³⁾, Nonne⁴⁾, and others. In Barkman's patient it led to feminism and frigidity⁵⁾. In women with encephalitic adiposity menstrual disturbances are not infrequent, sometimes even amenorrhea (Case 41).

¹⁾ Revue neur. 1922. 1024.

²⁾ Acta medic. scandinav. 1922. Vol. 56.

³⁾ Monatsschr. f. Psych. u. Neur. 1922. Vol. 50.

⁴⁾ Verhdl. deutsch. Gesellsch. inn. Medizin. 35. Kongress Wien 1923. p. 67.

⁵⁾ In my Case 51, there was cessation of libido. The same was found by Moulon, Colin, Lhermitte, (in a woman of 28 years, subsequent to a transitory phase of erotism).

A few of my patients had considerable loss of hair, both from the head, cilia, eyebrows, pubes, and axils (Fig. 1). In Case 55 there was a pronounced partial whitening of the hair of the head.

Personally, I have never encountered typical myxœdematous changes in chronic encephalitis, nor have I seen any such described in medical literature. Kennedy, Davis & Hyslop, Grosman, Gerstmann & Schilder, mention an exophthalmos, a phenomenon which in the least

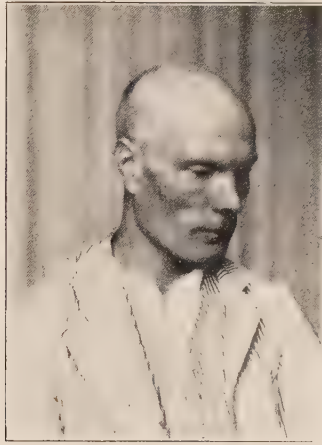


Fig. 1.

seems somewhat uncommon. In one single instance I myself have seen slight swelling of the thyroid gland, but never a pronounced Merseburg triad.

The cases of encephalitic pubertas præcox described, among others, by Stern⁶⁾, are extremely interesting. In my Case 14, the above mentioned boy of 13 years of age with precocious sexuality there was almost a macro-genitalism (Fig. 15).

The blood sugar determinations carried out in this department gave almost normal values throughout.

⁶⁾ Med. Klinik 1922. No. 27.

I have induced my late assistant, Dr. G. E. Schröder, to subject our chronic encephalitic cases to a more systematic examination as far as the neutrality regulation was concerned¹). In by far the majority of cases, of the most variegated clinical types, (Cases 4, 7, 9, 14, 21, 22, 23, 24, 32, 41, 53) that form of "dysregulatio ammoniaca" was found which Bisgaard, Nørvig & E. Larsen — by the application of a different method — have demonstrated in epileptics, and in some other patients with psychotic disturbances.

As is well known, Bisgaard and his pupils consider the cause of the ammoniacal dysregulation to be a dysfunction on the part of the glandulæ parathyreoideæ²). It has always seemed to me somewhat improbable that it should be possible so accurately to "localise" the disturbances of such a general function as the neutrality regulation of the body. All the more so, because in endocrinology there is a marked tendency now a days to seek the etiological factors more in polyglandular disturbances than in "mono"-dyscrinias. Dr. Schröder's investigations in our department here have further confirmed my doubts; for, "dysregulation" seems to be present in a large number of clinically heterogeneous types of disease (which, by the way, have no "tetanoid" components whatever, such as Chvostec, electric muscular phenomena, or the like). For the present I might therefore regard the dysregulation as a dyscrinal stigma, at most, but I would be prepared to believe that its origin should be

¹) A complete statement of the results of the "regulation tests" carried out with the patients in our department, has been published by Dr. Schröder in *L'Encéphale* 1924 no. 3 and 4.

²) Nørvig: *Undersøgelser over Stofskifteanomalier ved Psykoser I. Den saakaldte genuine Epilepsi*. København 1921 (Investigations into metabolic anomalies in psychoses I. The so-called genuine epilepsy. Copenhagen 1921.-). Bisgaard, Nørvig, Larsen, Henriksen: *Comptes rendus des séances de la société de biologie*. 1920—1921, and *Zeitschr. f. ges. Neur. und Psych.* 1922. Bd. 78; 1923. Bd. 83 and *Zentrbl. f. d. ges. Neur. und Psych.* 1922. Bd. 29.

sought for now in one, now in another of the endocrine glands, sometimes perhaps in several of them simultaneously if not in a central sympathetic lesion (compare below p. 299).

A form of nutritional disorder which not infrequently occurs at a late stage in parkinsonism (Mlle Lévy), but which may also be found, for instance, in more hyperkinetic forms of chronic encephalitis, is a pronounced emaciation, which may lead to a marked cachectic state. In several of my patients (Cases 8, 46, 55, 61, 62) this symptom was extremely pronounced; one of them (Case 46) had, at the same time, a "ravenous" appetite. In other patients too, we often get the impression that their excessive emaciation is not primarily due to lack of nutritional supply, but rather to internal, endocrinal or chronic toxic, or central nervous changes. Any more intimate chronological connection, for instance with fever, I have not seen.

BODY TEMPERATURE.

Opinions are extremely divergent regarding the conditions of temperature in chronic epidemic encephalitis. On the whole, chronic encephalitis may be said to be a nervous disease with a non-febrile course. It has however been stated by many authors — and is also confirmed by several of my case reports — that febrile phases or episodes may occur in the course of the disease, sometimes lasting for days or weeks at a time, sometimes even more persistently. Now and then the temperature may rise considerably; the moderate, subfebrile, temperature variations are however much more frequent (Lhermitte, Stern, Mlle Lévy, Gulstad). Sometimes there is a certain "periodicity", an "every other day" type; or, the variations set in at intervals of a fortnight or some months (Misch, Stern, and others); in

other cases we have more continuous subfebrile oscillations (Cases 28, 41, 46, 47). A fact which has struck me particularly in these temperature curves is that the figures for both morning and evening temperature very often remain at or above 37° C., and that the difference between evening and morning temperature is on the whole less than usual (Cases 28, 48), so that we have a "flat" temperature curve of a few decigrades oscillation. In Case 28 we have a periodical inversion of the temperature curve, the evening temperature being lower than the morning one, as has also been noted by Sicard in the acute stage of encephalitis¹⁾.

The terminal hyperthermia (Mlle Lévy) should, I suppose, be taken as an evidence of complications (bronchopneumonia, septic processes derived from bed-sores, and the like).

Coincident with these oscillations in temperature there occur occasionally modifications in the entire clinical aspect, appearances of new symptoms or aggravation of old ones, etc. In other instances there are true febrile relapses, such as, for example, in Cases 41 and 58. But, as will also appear from several of my reports, mere episodic rises in temperature associated with more or less sudden outbursts of neurological symptoms (Case 64) are, in my opinion, of considerable value in differential diagnosis.

However irregular and capricious the temperature conditions are in chronic epidemic encephalitis, I would recommend that the temperature should be taken daily (morning and evening), as a link in the chain of observations, in any patient who is suspected of (or reliably diagnosed as) suffering from chronic epidemic encephalitis.

¹⁾ *Revue neur.* 1921. — In Misch's patient there was fever (up to 41° C) only when the patient was awake, while the temperature fell to $37,1$, $37,2$, when the patient slept (especially at night).

NEUROLOGICAL TYPES.

Polymorphism is especially evident in the neurological types, and it is, therefore, difficult to classify these into any well defined groups; moreover such a classification would probably only possess a mere didactic value.

This polymorphism is caused not only by the fact that the dominating "syndrome", for example parkinsonism, may be blended with symptoms of a different anatomical localisation and due to different patho-physiological mechanisms; but also, by the great variability of the clinical picture, which is constantly undergoing change: some symptoms will disappear while others arise; an atonic-akinetic syndrome, for instance, may eventually pass into a more hyperkinetic one, or conversely, etc.

With this reservation I will attempt to classify my cases into three main groups.

1. Chronic encephalitic parkinsonism.
 2. Intermediary types.
 3. Extraparidal hyperkinesia.
-

1. CHRONIC ENCEPHALITIC PARKINSONISM.

This form of encephalitic "sequel" was that which first attracted the attention of clinicians, both on account of its great frequency (cf. above, p. 2) and on account of its characteristic clinical aspect which often strikingly suggests the classic paralysis agitans, Parkinson's disease.

Several of the writers who have been mentioned in this treatise have thoroughly described encephalitic parkinsonism. I shall call attention more especially to the excellent and exhaustive description of "les syndromes parkinsoniens", including the encephalitic one, which Souques gave at the meeting of the "Réunion neurologique annuelle" at Paris in 1921¹⁾. Mlle Lévy, too, in her thesis, describes these clinical types very clearly; Stern, in his monograph on encephalitis, does the same.

Just because the conditions found in this disease bear so great a symptomatological resemblance with Parkinson's disease, the "classic" paralysis agitans, it is not necessary to give here a further detailed description of its characteristics; it will be sufficient to state the main clinical features.

As has been previously mentioned, parkinsonism is that form of chronic encephalitis which relatively most frequently emerges directly out of the initial febrile phase, or which may be present with more or less pronounced symptoms during the acute stage. (Case 4)²⁾. An interval of shorter or longer duration may however also occur; in one of my patients there was an interval of five years. And, on the other hand, the acute febrile initial stage may totally fail to occur. In the cases where parkinsonism has such a completely "cryptogenetic" development, perhaps in patients approaching the customary age at which the classic paralysis agitans usually appears³⁾, it will readily be understood that the differential diagnosis may be extremely difficult (cf. p. 193).

1) Revue neurologique 1921.

2) Buzzard, S. K. Wilson were among the first to describe this "early parkinsonism".

3) According to Souques' statistics the "genuine" paralysis agitans makes its appearance mainly after the 40th year, and in by far the majority of cases, after the 50th, while the encephalitic parkinsonism is only rarely found in persons above 40 years of age. Compare also Mlle Lévy's statistics and Kn. Krabbe, Bibl. f. Læger, 1923, p. 355 (culmination towards the close of the 5th decennium)).

Encephalitic parkinsonism is perhaps most frequently a "paralysis agitans sine agitatione"; its main characteristic is the dystonic extrapyramidal syndrome, i. e. a steadily increasing muscular hyper-tonia, and rigidity. This rigidity may be localised (facial, mono- or hemiplegic (case 10), etc.); but more frequently it is general from the very onset or it rapidly becomes so, extending all over the muscular system of the body, often becoming as severe as in the classic paralysis agitans. At an early stage of the disease these encephalitic patients may assume the facial expression (amimia) and the attitude characteristic of paralysis agitans.

This progressive stiffening of the whole body, which eventually gives these patients the appearance of automata or "pillars of salt", is often accompanied by slowness of movement (bradykinesia), with a more or less pronounced limitation of the spontaneous movements (oligokinesia); in the late stages of the disease we may almost speak of an akinesis, cessation of nearly all the involuntary (automatic) movements, and an extremely limited power of performing, on demand, any of the voluntary movements¹⁾.

This sluggishness of motion and hypertonia are also usually evident in the gait of patients (bradybasia), not infrequently accompanied by anteropulsion or retropulsion, or by "hyptokinesia" (v. Sarbo)²⁾, a tendency to spontaneous running backwards, often beginning as an involuntary "bending backwards" (Case 13) or, for instance, it may be evoked if an attempt is made to raise the forward-bent head (Case 3). Owing to this anomaly several of Mlle Lévy's patients found a difficulty in doing their hair.

A symptom which is closely associated with muscular rigidity is akathisia (Haskover)³⁾, which is well known

1) One of my patients "begins by walking fast and ends by walking slowly".

2) Derived from *ὑπτίασμα*, bent together. According to Lhermitte the symptom is described by Trousseau.

3) Derived from *a* privativum and *Καθίψω* I sit.

also in cases of paralysis agitans (impatience musculaire, Brissaud), and to which attention has been called recently by Sicard, and R. Bing¹⁾: the patient cannot remain sitting on a chair, will constantly get up, take a few steps round the room, etc. These patients likewise often find it difficult to obtain rest while lying on their backs, because, owing to the gradually increasing fetus-like, doubled together, posture, they are unable to assume a comfortable position in their beds, and so, of course, their sleep becomes disturbed and restless.

A fundamental characteristic of extrapyramidal bradykinesia is the difficulty of passing from static to dynamic muscular function (v. Voerkom)²⁾. The fact helps to explain that voluntary or passively elicited movements sometimes stiffen into catatonic (cataleptic) attitudes (Fig. 5, 13, 20). This symptom, this motor inertia, may become extremely annoying to the patient during meals, in dressing and undressing, etc. The patient mentioned as Case 48 complained that, when she was doing her hair, "her hands remained fixed at the back of her head". The patient in Case 13 contracted a large burn in his right palm because he could not "free it" from a heating apparatus he had accidentally touched; on another occasion he burnt his right fore- and middle-fingers because he was unable to throw away a smoked cigar quickly enough³⁾.

¹⁾ Schweiz. med. Wochenschr. 1923. p. 1.

²⁾ Verger & Hesnard (L'Encéphale 1920; p. 409) speak of "le syndrome de viscosité motrice", C. & O. Vogt of "lack of denervation": The abnormal increase of tone, coincident with passive shortening of the muscles (Westphal's "paradoxal contraction", Strumpell's "fixation rigidity", Forster's "fixation contraction", Foix's "reflexe de posture"), is no doubt also of significance in the occurrence of catalepsy.

³⁾ The symptom reminds one of the "myotonic" perseverance in Thomson's disease. A myotonic, electric muscle reaction in striatal syndromes (including postencephalitic parkinsonism) has been observed by Soederbergh, Kleist Thomalla, Foerster, Lhermitte, H. Claude, and others, and was provoked by mechanical muscle irritation in our Case 60.

In young individuals this symptom, taken together with the other psychomotor and mental rigidity, will sometimes give rise to faulty diagnoses, dementia præcox, for instance, as was the case in my patient mentioned later on (p. 51).

The motor processes in encephalitic parkinsonism sometimes exhibit certain paradoxical conditions which, from a diagnostic point of view, it is of great importance to know.

Thus, while many automatic movements, for instance, the pendulous swinging of the arms associated with walking, will often disappear (Souques), we encounter, in other cases, a more ready performance of certain automatic muscular movements. Souques has thus described a "kinésie paradoxale"¹⁾: certain patients with parkinsonism, extremely rigid, unable to walk or to perform the simplest every-day movements, may momentarily, by certain external or internal impulses (emotional reaction, etc.), be induced to run, jump, or perform other rapid movements with the greatest ease.) Mlle Lévy records that one of her small encephalitic girls, who was not able to help herself in eating or dressing, could however "skip in a rope" and "play ball" with great adroitness. Meggendorfer, too, mentions these paradoxal "movement phases". I have myself witnessed a similar condition in a small girl with hemi-torsion spasm²⁾; cf. also Case 13³⁾.

An automatic iteration, a persistent repetition of the same habitual movements (taking the comb through the hair, wiping the cheek with a handkerchief, and the like) is mentioned by Haushalter⁴⁾. Such movements,

¹⁾ Revue neur. 1921. p. 559.

²⁾ A record of this case will be published later. Compare also my paper on "progressive, infantile torsion spasm", Revue neur. 1921, p. 953.

³⁾ Lhermitte mentions H. Colin's case, a patient with pronounced parkinsonism who, during somnambulism, proved to be "agile et libre de ses mouvements"; v. Economo likewise mentions the improvement of the parkinsonian rigidity towards evening.

⁴⁾ Revue neurologique 1922 p. 476 ("répétition automatique").

too, remind one of those found in catatonic forms of dementia præcox. But, in regard to both this automatic repetition and the catatonic rigidity, it is without doubt a question of different patho-physiological mechanisms, as the movements found in dementia præcox patients seem to be caused predominantly by psychic factors (Bleuler), compare below p. 320.

There seems to be no strict parallelism between the degree of hypertonia and the degree of motor sluggishness; probably the patho-physiological mechanisms governing these symptoms are partly different (F. Stern, and others). The hypertonia may be slightly pronounced, or almost wholly absent, notwithstanding the presence of a considerable bradykinesia (Case 9), or akinesia (Lhermitte); less frequently the opposite is found to be the case. Or, the hypertonia may be localised to the facial and cervical muscles, to one arm, etc., while the sluggishness of motion is general, etc.¹⁾ This dissociation, however, belongs essentially to the earlier stages of encephalitic parkinsonism; if there is no general improvement of the disease, both the muscular rigidity and the bradykinesia will increase to a maximum during the later stages.

As has already been pointed out, the encephalitic parkinsonism is very frequently a "paralysis agitans sine agitatione". That is to say, there may be total absence of tremor, as in two thirds of Souques', and more than half of Stern's patients. Or, if tremor occurs at all, it does not set in until long after the bradykinetic-hypertonic symptoms. Often, it remains moderate, not rarely restricted to definite parts (monoplegic, hemiplegic, shaking of the head, etc.). It spreads slowly, or not at all; and, after some time, it may wholly disappear.

The so-called tremor at rest ("pill-rolling", etc.) which is a characteristic feature in paralysis agitans, is of far

¹⁾ Mlle Lévy describes a case of almost pure hemihypertonia exclusive of other parkinsonian symptoms (Case 61).

less frequent occurrence in encephalitic parkinsonism than the forms consisting of a coarser arhythmic shaking or oscillation which only occur with voluntary movements (action tremor), or when the patient attempts to hold an arm or a leg uplifted without support (static tremor). At any rate, it is nearly always the case, and my own experience bears this out, that an existing tremor of the muscles at rest is aggravated by attempts at action (without, however, increasing towards the aim, such as found in disseminated sclerosis); in classic paralysis agitans active movements may, as is well known, cause lessening of, or complete cessation of, the tremor.

The patient's handwriting often affords a fine illustration of the tremor; in one of my patients the tremor in the right hand and arm increased to a violent, almost "choreatic shaking spasm". Still more characteristic than these coarser irregularities in the handwriting, or the zig-zag outlines of the letters, is perhaps the micrography encountered both in classic paralysis agitans and in encephalitic parkinsonism¹⁾. The decisive causative factors are here, no doubt, the "stiff" fingers, the limited slow movements of hand and arm: one of my patients, a young clerk, suffering from a rather severe attack of parkinsonism, who now writes his letters two or three times as small as he used to do before he became ill, says that he has the feeling that he cannot "make the pen go round"; that is to say that all the finer co-ordinate muscular movements of the fingers are very sluggish and defective. Moreover, the effort of carrying the pen further towards the right is impeded by the rigidity in the hand and shoulder muscles, so that the letters are rapidly "fused together" (Fig. 2).

If the motor sluggishness (and hypertonía) involves the muscles of the mouth, we get difficulties of mastication.

¹⁾ Froment: *Rev. neur.* 1921. p. 637; Bing, loc. cit. Froment's patient was only able to write letters of normal size, when, like a pupil at school, he wrote between double lines.

lion¹⁾, while the act of swallowing is only affected in very severe or complicated cases.

Disorders of speech will occur sooner or later in these patients, primarily a bradyphasia, corresponding to the other sluggishness of movement, and consisting in a drawling, monotonous, dull voice, sometimes somewhat explosive. Furthermore, there is often a pronounced oligophasia, a laziness of speech (Mlle Lévy),

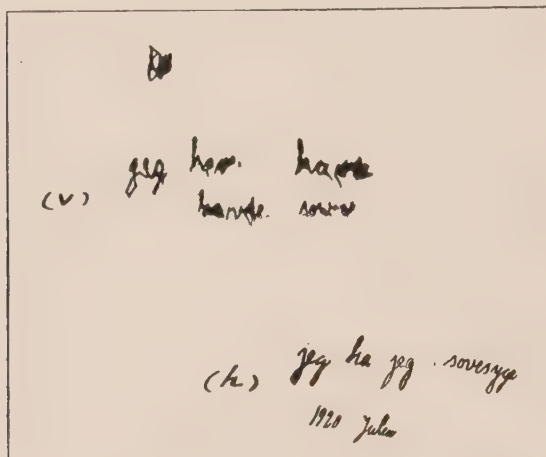


Fig. 2.

the patient confining himself to using a minimum of words or the shortest possible phraseology; a phenomenon which, during transitional or terminal stages of the disease, may lead to more or less persistent mutism (Case 13). Here, however, we also encounter paradoxical states: H. Claude has described a paroxysmal tachyphemia, crises of chattering, with stereotypy of words, reiteration of the same word, or the same phrase, frequently at an increased rate and in a strained manner.

¹⁾ One of my patients had a pronounced "bradymasia", increasing during the meal.

The palilalia, described by Souques in 1908 in patients with true shaking palsy, and by Pierre Marie & Mlle Lévy in 1922 in connection with encephalitic parkinsonism¹⁾, seems to be closely related to the above-mentioned phenomenon. Here, too, the patient, apparently acting under an involuntary and irresistible compulsion, will repeat single words or short phrases up to twenty times and even more. In one of Pierre Marie & Mlle Lévy's cases this disorder ended in an aphonic, purely "motor" palilalia; after repeating the word or the phrase several times the lips continued to form the words without a sound being heard. This palilalia may likewise develop into mutism²⁾.

Such grotesque disturbances of speech may occasionally — more especially in children and youths, or in women, convey the impression of being "hysterical", for it holds good in regard to these troubles too that, under certain conditions, they can be inhibited voluntarily or brought to an end; and moreover, it is characteristic also of these encephalitic speech disorders that they primarily involve voluntary speech, while they decrease, or wholly disappear, in more automatic speech (Tinel), such as, for instance, recitation, reading, exclamation during states of agitation, and the like, conditions which have also been pointed out by Babinski³⁾. We have here a "kinésie paradoxale" similar to that described by Souques.

In parkinsonism, more especially in forms exhibiting "pseudo-bulbar" symptoms, etc., spasmodic weeping and explosive outbursts of laughter are of frequent occurrence, and often intensify the impression of "fatuity" made by the patient. These symptoms may, of course, also be found in other forms of chronic encephalitis.

¹⁾ *Revue neur.* 1922. p. 67.

²⁾ The palilalia to a certain degree reminds one of the logoclonia found in connection with certain senile cerebral lesions (Alzheimer's disease, Pick's atrophic parietal syndrome).

³⁾ *Revue neur.* 1922. p. 74 (cf. my Case 26).

The forms of respiratory disorders which not infrequently occur in encephalitic cases, also sometimes in those with parkinsonism, will be described later.

Parkinsonism, i. e. the triad consisting of "motor sluggishness, hypertonia, tremor", is characterised also by the negative facts that there is an absence of pyramidal tract symptoms (true palsies, hyperreflexia (to the point of clonus), Babinski reflex), absence of sensibility or sphincter disorders, absence of ocular symptoms (palsies, pupillary disturbances), etc.

Encephalitic parkinsonism, however, is seldom found "pure"; in my cases, at any rate, only in two or three of them at most (Case 3). In by far the majority of my patients, even where parkinsonism is the predominant feature, there is an addition of other nervous symptoms not inherent to parkinsonism, as will be fully illustrated by my cases.

Moreover, parkinsonism may — with more or fewer of its symptoms — form a partial syndrome in morbid conditions which are primarily characterised by other syndromes.

And, finally, even though parkinsonism in numerous cases remains the dominating and constant feature in these morbid conditions, it may, in other cases, give way to, or be overshadowed by, nerve symptoms of an essentially different character: athetosis (v. Economo, Foerster), myoclonias, and the like (Pierre Marie, Babinski, Trétiakoff & Bremer; my case 7), hemi-paresis (Häusalter), etc.

To illustrate the general picture of encephalitic parkinsonism sketched in the foregoing pages, some records of cases will now be given.

Case 3. Woman, aged 46, under the care of my department March-August 1923.

Previously healthy. In 1919 she had a few days' attack of fever ("influenza"). In 1922 a slowly developing muscular rigidity and slowness of movements set in.

Then a typical mask-like face and parkinsonian attitude (Fig. 3). Tremor in the arms when resting; pronounced muscular rigidity with katonoid arrest of movements; bradybasia and microbasia; retropulsion, pitching backward when attempting to raise her forward-bent head.

No symptoms from the pyramidal tracts; no myoclonia. Pupillary reactions normal. Some adiposity, but no other vegetative disorders. Blood pressure 130 mm. The urine was free



Fig. 3.

from albumin, sugar and urobilin. Spinal fluid showed: cells 0/3, globulins 0, albumins 7—8; Wassermann reaction negative in both serum and spinal fluid. Temperature on some evenings 37.8. No tachycardia.

Case 4. Woman, aged 34, admitted to my department 23d January 1923, whom I had however had an opportunity of examining in August 1922 (on account of her request for an invalid pension).

Previously healthy, she contracted the „Spanish disease” in February 1922, lay a couple of months with high fever, not specially drowsy; no squinting, no motor restlessness. Towards

the end of her confinement in bed a tremor of the right leg developed, later of the right arm, gradually also a little tremor of the left limbs. At about the same time she noticed stiffness of the limbs, which increased slowly, extending to the muscles of the back, neck and face. Her movements became slow, difficult, "she walked like an old woman", gradually she became unable to do any housework. For a time there was weakening of the eyesight, she could not see to do needlework nor to read the



Fig. 4.

newspaper, but could still see things at a distance. She grew obese, had increased 10 kgs. in weight before her admittance here; suffered for some time from polydipsia, for some time also from excessive perspiration. Constantly regular menstruation. Now and then transient dedolations in the limbs.

She is rather stout, strongly built, weight 79 kgs.; plenty of adipose tissue. Face extremely immobile, excessive bradykinesia and bradybasia. Typical parkinsonian attitude (Fig. 4). Moderate general rigidity. Some coarse, arrhythmic tremor in the right hand and fingers at rest, also a little in the right foot; in the left hand rather a little action tremor. During mime-

tic movements there is medium to fine tremor of the facial muscles; the tongue, too, tremulates excessively. Lighter grade of bradyphasia; no dysmasia or dysphagia. At times bradypnea (13—14 respirations a minute). During periods of 2—7 days, tachycardia with a pulse rate of up to 112 a minute has been observed.

No spasmodic laughter or weeping. No pareses, tendon reflexes normal, bi-lateral Babinski reflex. No sensibility or sphincter disturbances. Slight convergent strabismus; pupillary reactions to light and on accommodation preserved; ophthalmoscopy showed normal conditions.

Spinal puncture showed cells $\frac{1}{3}$, globulins 0, albumins 7—8; Wassermann reaction negative in serum and spinal fluid. — Blood sugar 0,058—0,064. Diuresis below the normal. The urine was free from albumin, sugar or urobilin. She was a dysregulator. The temperature was normal during the whole stay.

In this otherwise very typical picture of parkinsonism we have, however, a few symptoms which are not inherent to classic paralysis agitans: the bilateral Babinski reflex, betraying a certain involvement of the pyramidal tracts; and certain ocular phenomena, the persistent squint, and the transitory impairment of vision which, according to its manifestations, undoubtedly must be interpreted as an accommodation paralysis.

In the following reports, also, the parkinsonism is not "pure"; in some of the cases the pronounced psychic disturbances are of special interest.

Case 5. Woman, aged 39, married;¹⁾ previously healthy. In July 1918 and June 1919, an attack of fever which lasted a few weeks: temperature up to 39° C, headaches, drowsiness, no certain mesencephalic signs. In September 1920 diplopia was suddenly experienced (paresis n. abducent. sin.), temperature up to 39, headaches, confusion, hallucinations, severe choreatic unrest in arms and legs; herpes labialis; duration a few weeks, then good health for some months; after which period headaches, sleeplessness, palpitation, motor inertia, gradually tremor of the hands, psychic torpor, hypocondriacal ideas (cancerophobia), increasing depression, and, in June 1921, tentamen suicidii (with gas),

¹⁾ Shown in the Neurological Society of Copenhagen 30th November 1921.

on account of which she was admitted to my department from 1.—7. June: Serious poisoning, somnolence, etc.; though she soon recovered. At that time, however, she already displayed rather a pronounced Parkinsonian syndrome (amimia with “greasy-face” and salivation, rigidity, bradykinesia, bradybasia, no distinct tremor). Indication of paresis of conjugated eye movements upward, normally reacting pupils; ophthalmoscopy showed nothing abnormal; no symptoms from the pyramidal tracts. Lumbar puncture showed cells 2/3, globulins 0, albumins 10. Wassermann reaction in serum and spinal fluid negative. Slight glycosuria. She was then discharged, but a



Fig. 5.

week afterwards she was again admitted — owing to a new attempt at suicide (gas) — with slight poisoning. The motive for her suicidal attempt was the same as before: “she was unhappy because she could not move her legs”.

She then stayed at the department until June 22d 1922, her disease steadily progressing: growing stiffness of the whole body, the head stiffly fixed downward towards the left; she lay almost motionless in bed, had typical Parkinsonian attitude when out of bed, marked bradykinesia; the spontaneously or passively moved arm often remained in the same cataleptic posture (Fig. 5). Slight tremor of hands and fingers at rest; pronounced and moderate action tremor; trembling of the muscles of tongue and lips; slight, irregular shaking of the head; some

myocloniform unrest in the abdominal muscles. Considerable bradyphasia. Involvement of the pyramidal tracts not certain. The reaction of the pupils to light gradually became very sluggish. Eye movements free, ophthalmoscopy showed nothing abnormal. On two occasions lumbar puncture showed considerable hyperalbumosis (30, ad modum Bisgaard), with normal globulin and cell figures. The glycosuria vanished.

The depression gradually gave way to a rather marked bradyphrenia; but true dementia did not appear.



Fig. 6.

Case 6. Girl, aged 18¹): "Influenza" without positive cerebral symptoms in 1918. In April 1920 diplopia suddenly developed (paresis of both recti interni), drowsiness, headaches, dizziness. She continued to be sleepy, lacks energy, is uncleanly, dribbles, has irrelevant fits of laughter, outbursts of anger; she develops a desire to tease, to pilfer money (and other things) at home. She remained at the department from 18th October to 16th December 1921. Typical Parkinsonian syndrome of me-

¹) Shown at the meeting of the Neurological Society of Copenhagen 30th November 1921.

dium intensity (Fig. 6), though only slight tremor. The pupils do not react to light and on accommodation. Ophthalmoscopy showed normal conditions. Babinski reflex on the right side, otherwise no symptoms from the pyramidal tract. Psychically she is rather dull. Lumbar puncture showed normal figures for cells and albumins, Wassermann reaction negative in both serum and spinal fluid. — Her condition improved somewhat.

The following case is of a peculiar interest on account of its "cryptogenetic" onset, and the comparatively rapid development of the Parkinsonian syndrome.

Case 7. Agent, aged 39, admitted 2nd March 1923 (on account of "paraparesis spastica"). His father had been epileptic. He himself previously of good health; denies syphilis and alcoholism. No positive information as to "Spanish disease" or the like. Still, it may be mentioned, that in March 1923 the patient's brother applied to the department for out-door patients at the Rigshospital, complaining of weariness, dullness of thought, frequent fits of violent giddiness, which symptoms he attributed to an "influenza" in January 1922, when he was in bed for about a week, with high fever and somnolence. The present illness of our patient developed gradually during the month preceding admittance, with disorders of sleep, general feeling of weariness, increasing slowness of movements, and bradybasia. The face gradually became more and more immobile and "mask-like", speech slow, monotonous, with slightly nasal accents; he became dull at his work; no indication of true somnolence. During the last few weeks tremor of the right leg has appeared. Diplopia, headaches, giddiness, vomiting, and subjective febrilia absent.

He is big, strong, somewhat obese, rather bald; face very mask-like, immobile; slightly "greasy-faced" (Fig. 7), carriage stooping, somewhat in the manner of an old man, the arms slightly flexed, the hands in a slightly "obstetrical" position; they do not swing in rhythm with the body when walking. The gait is slow, with small, dragging steps; very marked retropulsion. Irregular, moderate rocking tremor of the head, when he sits erect, but also a little when the head rests on the pillow; no tremor of arms or legs.

Upper eye-lids very drooping, but they can be raised almost entirely. Slight impairment of convergence movements of eyes (he declares that he sees double when he reads, for instance, but not when he looks about him in the room). Nystagmus absent. The pupils react promptly to light, but show strikingly

diminished reaction on accommodation. Visual fields were found to be normal. Functional otologic tests showed nothing abnormal. Perhaps slight paresis of left muscles of the face. No paresis of tongue or palate; no fibrillation of facial or lingual muscles. Speech somewhat drawling, monotonous.

No sure paresis of extremities, slight hypertonia in the arms and, especially, in the legs. The right patellar reflex more lively than the left; left-sided, slight ankle clonus; bilateral (?) Babinski reflex. Abdominal reflexes absent. No disturbances of coordina-



Fig. 7.

tion or sensibility; sphincter functions normal. Respiration type and pulse normal. Psychically he is intact. Lumbar puncture: cells $18\frac{1}{3}$ (small lymphocytes), globulins 1, albumins 10; Wassermann reaction (serum and spinal fluid) negative. No albumin, sugar, or urobilin in the urine. — Blood pressure 160 mm. The patient is a dys-regulator. — Temperature normal, until the patient contracted pneumonia on the 10th March; there ensued great increase of muscular stiffness, the right leg drawing itself more and more up into flexion contracture, partially through cloniform jerks; there is, moreover, a persistent, pronounced though irregular tremor of moderate rapidity of the toes, and small, myocloniform jerks in the right orbicularis oculi. The tremor of the head also somewhat increased.

For three to four weeks his general health was considerably lowered. Following on the abatement of the pneumonia the temperature again became normal, though tachycardia persisted (up to 128 a minute). A very minute examination of the heart revealed no signs whatever of an organic heart affection.

The mimetic stiffness had diminished a little, but the Parkinsonian face and attitude continued to be very pronounced; marked bradykinesia and bradybasia; some bradyphasia. The rigidity had somewhat diminished, especially in the legs, so that he was able to move about a little better on the floor. A little fibrillation in tongue and lips, no tremor in the arms at rest, but marked swaying in action. Tendency to Babinski reflex on the left side. He had been treated with argotropine.

When he left the hospital on July 7th 1923, he could walk rather fast, the bradykinesia had abated and so had the bradyphasia. More especially, the rigidity and oligomimia had improved considerably. On January 26th, 1924, he was once more examined. The Parkinsonian symptoms were now very slight, but, still, his face wore a somewhat masklike expression, and in the legs there was a rather marked hypertonicity, with ankle clonus and a tendency to extensor response in the left foot.

Slight myoclonic jerks had begun to appear in the muscles of the jaw, most frequently at night. In the daytime his chin was usually drawn a little downwards and inwards, and sometimes, too, he would yawn twenty times in succession. He looks rather short-necked, the muscles of the neck being markedly contracted and hypertonic.¹⁾ Type of respiration somewhat polyneic and snappy; pulse rate up to 120.

On February 1924, he again came to the hospital, for another course of argotropine treatment. The spasms in the neck still exist, and he still has spells of yawning, etc.. In the right thigh, too, he has frequent "starts" and some pain. Now and again, diplopia has been present. He complains of a feeling of numbness in the two ulnar fingers of the right hand.

General appearance slightly Parkinsonian. Contraction of muscles of the neck, retraction of chin, etc., as described above. Moreover, the angles of his mouth are constantly depressed, by a tonic spasm in the muscles, giving his face a rather piteous expression. In the muscles of the chin some slight myoclonic jerks may sometimes be seen. There is no jerking of the tongue, no marked troubles of speech or of swallowing. In the muscles of the right thigh numerous myoclonic jerks are constantly seen; there is a marked hypertonia of the right quadriceps.

¹⁾ He has had to wear lower collars since he became ill.

Myoclonias are found nowhere else. No true pareses; knee jerks exaggerated, and a bilateral Babinski reflex may sometimes be elicited. Ophthalmoscopic examination showed normal eye grounds and pupillary reactions to light and on accommodation, normal acuity of vision and visual fields, latent, alternating, divergent squinting. After reading a few minutes, he complains of diplopia.

In the spinal fluid were found cells 2/3, globulins 0, albumins 9—19, the Wassermann test being negative in the blood and the spinal fluid. No pathological findings in the urine, no polyuria. Temperature on evening of admission 38.2. Rate of pulse up to 112. A thorough examination of the heart does not reveal any organic lesion; neither are there any definite pathological changes in the lungs.

In this patient, the regression of the parkinsonism and the subsequent occurrence of myoclonic symptoms is very interesting, denoting the persistence of an active, encephalitic process. In regard to the "yawning tics", this patient bears a close resemblance to those described in Case 10 and 12.

Another of my cases who revealed a purer form of parkinsonism was a man, aged 26, who was admitted to my department for mental diseases under the diagnosis of "dementia præcox", apparently on account of his slight Parkinsonian syndrome (slight rigidity of carriage (Fig. 8), oligomimia, sluggishness of movement and speech, scarcely noticeable tremor in the hands at rest, together with a pronounced bradyphrenia, a mental and physical dullness, which had made him impossible at his work. The patient himself was able to realise his feeling of "stiffness"; observations showed no signs whatever of schizophrenia. The disease seemed to have its origin in a misinterpreted epidemic encephalitis in 1921¹⁾.

In the following patient "parkinsonism" is chiefly evidenced by a marked and extensive tremor; there are, however, certain symptoms of another kind, transitory or lasting, which make the picture rather polymorphous.

¹⁾ The patient in Case 10, too, was admitted with a diagnosis of dementia præcox, while the patient in Case 26 was certified as a case of "melancholia".

Case 8. Hospital night-nurse, single, aged 46, admitted to the department 23d February 1923. Her mother's brother suffered from "shaking" (tremor) at an advanced age; a brother had diabetes. Her right hand has always been inclined to shake. No serious bodily troubles. Menstruation regular.

In February 1922 "influenza", she lay at home for three weeks, "slept through the greater part of three days", had fever up to 39.5°C. , and suffered from diplopia; no definite motor unrest.



Fig. 8.

Since then she has not been quite well: tremors occur, slowly increasing and spreading "all over the body", mostly affecting the head and hands; pains in the head, "as if it was out of joint", and in the left half of the face; general weariness, sleeps badly. In December 1922 "swallowing difficulties", i. e. pressure in cardia; backaches; since then a perpetual feeling of "a lump in the throat". She has an inclination to "sigh" and "yawn", in long spells; no other respiratory paroxysms. During the last months of 1922 she suffered from excessive thirst and polyuria (which also disturbed her sleep at night).

She says she has grown very thin (from 75 kgs. down to 59 kgs.). No menstrual disturbances.

In November 1922 she was treated at Balder's Hospital, and subsequently in the III department of the Municipal Hospital, whence she was removed to this department. Glycosuria was then found, occasionally very pronounced, occasionally in a lesser degree, sometimes disappearing altogether; there were, in addition, a great many of the neurological symptoms described below. She slept badly, and became more and more depressed and anxious.

Examination revealed that the patient was thin and emaciated; weight 59 kgs.; extremely immobile face; rather slow movements, no definite hypertonia; speech inclined to be breathless and jerky.

In the resting or raised head irregular, rapid tremors of moderate intensity are apparent at nearly all levels, gradually extending to the whole body. Rapid, rhythmic tremor in the hands and legs at rest. By voluntary movements the tremor is not only greatly increased, but it becomes also more marked and jerky. Finger-to-nose test provoked decidedly irregular flinging movements in both arms, particularly, however, in the right arm, ending almost in "motor delirium". The patient cannot keep her fingers on the tip of her nose.

In the pectorales there was some moderate, fascicular vibration, in the abdominal muscles now and again small, faint myoclonic side-jerks of the umbilicus. Respiration type normal; hiccoughing, yawning, sighing, were not observed here.

No paresis of face, arms or legs; increased patellar and ankle reflexes, without clonus; right plantar reflex of flexor type, left somewhat dubious. No paresis of eye muscles and no nystagmus. Left pupil twice as wide as the right; pupillary reactions preserved. Ophthalmoscopic examination revealed nothing abnormal. In the left trigeminal region hypæsthesia and hypalgesia could be demonstrated.

Spinal puncture: cells 3/3 (small lymphocytes), globulins 0, albumins 9—10; Wassermann reaction in serum and spinal fluid negative. The urine was free from albumin and sugar (repeated tests), diuresis varying, though generally normal figures; temperature curve "flat", pulse rate a little accelerated¹⁾. She is a dys-regulator.

Psychically she was to begin with agitated, anxious, unhappy; saw people, heard them sing lampoon songs about her,

¹⁾ As to her vasospastic attacks, see p. 25. During a later stay in the ward, in Nov. 1923, there was a pronounced bradycardia.

wept, ran to and fro; at times she was rather hazy, chattering. Gradually her mind became clearer, though a good deal of uncertainty and erethism still remained, especially during the examination, when there was a violent increase of tremor.

This case is also of interest because, at an advanced stage of the chronic encephalitis, a pronounced psychotic phase set in, manifesting itself as an exacerbation of the general nervous symptoms which had persisted for some time; a corresponding aggravation of the neurological symptoms, rise of temperature, or the like, could, however, not be found.

Case 9 is interesting not only on account of its polymorphism, but especially because the patient's epidemic encephalitis had evidently set in during her pregnancy, and here we had an opportunity of watching her during the initial febrile stage, when several neurological symptoms caused us to diagnose the case as "encephalitis infectiosa".

Case 9. Married woman, aged 30, admitted the first time 2nd May 1920, removed from the maternity department of the Rigshospital.

Previously of good health; she had given birth to children in 1914 and 1916, without psychic disturbances supervening. The present pregnancy normal until 18th April 1920, when she suffered from violent pains in her chest and arms. After manual dilatation of the orificium uteri and pituitrin injection she gave birth to a living child May 1st, 1920. She now became sleepless, inclined to cry, had depressive delusions, strong hallucinations. Rise of temperature (38°) on one occasion after delivery; no albuminuria; no excessive hemorrhages or other symptoms of septic infection.

In the ward, she seemed at times harassed, cried, became dull, answered questions reluctantly; and, at other times, she was restless, anxious, with a tendency to leap out of bed; there was no ground to believe that she had hallucinations. Stethoscopy normal. Abdomen normal, uterus well involved, lochia not putrid. No albumin, sugar, pus, blood, or urobilin in the urine; microscopy revealed a few granular cylinders and a few leucocytes. The temperature curve oscillated irregularly; evening temperature up to 39.1° . Pulse between 100 and 136, during high fever slightly irregular.

Right pupil twice as wide as left, both reacting well. Eye movements appear slightly impaired in all directions, but there are no isolated palsies. Slight nystagmoid tremor of eyeballs in extreme positions. After a few days, a marked left-sided facial paresis set in. Spinal puncture showed: cells 62/3 (lymphocytes), globulins 1, albumins 10. Having regard to possible intra-uterine complications the patient, whose state was almost unchanged, was removed to the surgical department of the hospital on 29th June.

On the 16th February 1923 she was readmitted here. She has continually suffered from fatigue, and has often been very depressed and anxious; frequently had headaches. Sleep fairly good. No subjective fever attacks. In 1921 she had experienced shaking, or "muscular quivering" (not "jerks") in arms and legs, in left side of face and in the lumbar region, ("she could feel it with her hand"); in the left shoulder, however, the "shaking" was so violent, that the arm was moved slightly forward and upward at the shoulder joint. Increasing motor sluggishness set in almost at the same time. For a couple of years she had some impairment of vision ("as if she walked in a cloud of smoke"); frequently diplopia; and gradually her eyes became "stiff".

No difficulties of speech or swallowing, no paresis of the extremities. She states that her weight has increased considerably (from about 48 to about 66 kgs.), and, that she has lost a great deal of hair. Menses regular. No polydipsia or polyuria.

Psychically her behaviour in the ward was almost natural, she was not particularly lethargic. Looks strikingly matronly; is rather obese, face somewhat congested. Her hair (originally very abundant) has now grown much thinner; axillary and pubic hair growth is very scanty. Skin not myxedematous. Gl. thyreoidea not palpable.

No exophthalmos. Left pupil larger than right; reactions to light and on accommodation are preserved. Diplopia corresponding to the paresis of right n. abducens, with manifest strabismus. Moderate horizontal nystagmus, when looking in both sideward directions. Eye grounds, fields of vision, normal.

Slight paresis of left angle of the mouth. Myoclonic twitching or small jerks in left orbicularis oculi, left cheek, both angles of the mouth, and the muscles of the chin.

Speech somewhat low-pitched, a little difficult (Russian Jewess).

The tongue is decidedly atrophic, predominantly in the left half, with mounds, wrinkles and concavities toward the left, strongly fibrillating, small myoclonic jerks, no paresis. Palate free; pharyngeal reflex preserved.

Slightly increased muscular tone in the arms, more especially in the left one; movements are performed somewhat slowly. No definite pareses. Tendon reflexes brisk.

There is also some hypertonia in the legs; pronounced slowness of movement. Gait slow; some tendency to retro-pulsion. No pareses, brisk tendon reflexes without clonus, plantar reflex on the right side with slight tendency to dorsal flexion; normal on the left side.

When she sits erect or gets up, there is much shaking of the head, predominantly rotatory; no static swaying of the body. Now and again myoclonic jerks in the left platysma, a little "vibration" in the clavicular insertion of the right sternocleidomastoid, some rapid myoclonic jerks in the left pectoralis major. No distinct myoclonic unrest in the abdominal or dorsal muscles; the abdominal reflexes are present.

When at rest, there is moderate to rapid, fairly rhythmic tremor in the left hand and fore-arm, less, and only episodically, in the right, not increased by intentional movements; in the lifted arms, especially the left one, there is violent, coarse, static oscillation. True ataxia absent.

Some vibratory lateral tremor of both feet; now and then small myoclonic upward-jerks of the right patella; in the left vastus femoris, a little fascicular quivering without motor effect. Ataxia absent.

Sensibility, and sphincter functions, undamaged. Temperature, pulse, and respiration, normal. Diuresis strikingly diminished. No albumin or sugar in the urine; slight urobilin reaction. Hemoglobin (Sahli) 65 %. Blood cell count: 4,100,000 erythrocytes; leucocytes 10,600, of which 64 % were neutrophilic, 0,75 % eosinophilic; large and small lymphocytes 27 %, myelocytes 8 %, mast cells 0,25 %. Index 0,81.

The patient was a dys-regulator¹⁾.

She was discharged 27th March 1923, having but little improved.

She was again admitted to my department November 20th 1923. Her condition had remained almost unaltered. Such were also the findings at the neurological examination, except for a slight impairment of the left abducens. The pupillary reactions to light and on accommodation were still well preserved; eye grounds normal. Now and then, there was a slight bradycardia, while the temperature was normal. She was given an argotropine treatment.

¹⁾ Spinal puncture was not performed, because the patient would not come to the hospital unless she was spared that operation.

Case 10. In this case we have to deal with a hemiparkinsonism. The patient was a youth of 21 years, who was in the hospital for the first time during the summer of 1920. There was no reliable history of a febrile period. For about two months before his admission he had been a little queer and had revealed grimacing movements in the face. A few days before he was taken to the hospital he had a fit of generalised spasms, without loss of consciousness, no biting of tongue or involuntary micturition. At night, he sometimes became slightly delirious. In the ward his body and limbs were in a state of constant motion, with irregular, incoordinated, choreatic jerks, increasing on voluntary movements. In addition, myoclonic jerks were seen in the left limbs. No unrest of facial muscles or of tongue, and no ocular symptoms were observed. Sometimes he would sigh, or the respiration would become "snappy". There were no signs from the pyramidal tracts. He was slightly drowsy, and now and again a little delirious. On admittance, his temperature was 38.4° , while on two other occasions it reached 37.8° . The involuntary movements having disappeared, he was discharged after a stay of about a week.

Since then no myoclonic or choreatic symptoms. Sometimes his left arm would shake rather violently. Now and again, his mouth would remain half opened, without his being able to shut it; at this, he would sometimes "yawn". His movements have gradually become more languid, more especially his gait. This fact has also been noticed by those around him, who will frequently ask him "to hurry up". He has suffered somewhat from thirst and from polyuria, having to void urine every 3 hours. He has lost about 6 kgs in weight. He once had a swoon. Sometimes he sees double for some hours.

He was again admitted to my department February 22nd, 1924. He is a little bradyphrenic, rather slow of speech, also slightly bradykinetic. The face shows some oligomimia.

The tonus of the muscles of the left arm and leg is moderately increased; no hemiparesis; tendon reflexes moderately brisk, no Babinski reflex. There is a marked left-sided tremor in the limbs at rest, increased on static function and on voluntary action, especially when resistance is offered. In the left forearm and the left thigh some few myoclonic jerks are seen. The lips and the tongue are slightly fibrillating.

Pupils dilated, equal of size, react well to light and on accommodation. Movements of eyes, visual fields, eye grounds, normal.

In the ward he has had occasional fits of yawning, without any other respiratory troubles.

In the spinal fluid were found 9/3 cells, 0 globulins, 6 albumins. The Wassermann reaction is negative in blood and spinal fluid. The temperature has been normal throughout his stay in the hospital, as also the rate of the pulse. The diuresis is rather below the normal (480—800 ccm); no pathological findings in the urine. His general appearance is virile.

In the following case, the chronic phase of the disease appears as a direct continuation of the initial stage. Here, too, the parkinsonism *s. s.* becomes highly complicated, not only with milder hyperkinetic symptoms (myoclonic movements), but especially, with a marked characterisation of pseudo-bulbar symptoms, thus reminding one of the cases described elsewhere by v. Economo, Moulon, H. Colin & Lhermitte¹⁾, Lévy-Valensi & Schulman²⁾, Sicard & Paraf, and others.

Case 11. Male, aged 57, admitted to my department 15th December 1921, discharged 20th May 1922. "Gravel" three years ago. 26th October 1921 he was suddenly taken ill with fever up to 39.6°, headaches, vomiting, deliria. Admitted to the medical department of the hospital. The fever disappeared after four days. He was apathetic, somnolent, at times delirious. Speech slow, thick. The right pupil larger than the left one, both reacting to light; no apparent ocular palsies; ophthalmoscopy showed normal conditions. Spinal puncture: cells 2, globulins 1, albumins 10; Wassermann reaction negative in both serum and spinal fluid.

The urine contained albumin, blood, pus, numerous red and white blood corpuscles, granular cylinders. Blood pressure 145—150 mm.

In my department he appeared to be clear-minded, but rather bradyphrenic. His speech was bradyphasic, though at the same time highly dysarthric, thick and "choppy", sometimes to the point of being unintelligible. No aphasic disturbances. Expression of the face very immobile, staring in open-mouthed surprise; excessive salivation. Some explosive outbreaks of weeping.

Ptosis on both eyes, with over-acting of frontales; otherwise no paresis of the eye muscles. The facial muscles strikingly immobile (paresis? — rigidity?). No paresis of tongue or palate. No labio-glossal atrophy or fibrillation.

¹⁾ Annal. méd.-psych. 1922 p. 53.

²⁾ Revue neur. 1920 p. 1260.

Pupils equal, reacting to light and on accomodation. No corneal pigmentation. Eye grounds normal.

Considerable rigidity of arms and legs; no paresis; increased tendon reflexes without clonus; now and then indication of Babinski reflex on the left side.

No sensibility troubles. No tremor at rest, but violent shaking during voluntary movements, and coarse static oscillation in arms, legs, and head. Gait inclined to be "cerebellar-reeling". Romberg's sign absent.



Fig. 9.

Spinal puncture 22nd December 1921 showed: cells 7/3, globulins 0, albumins 15—20; Wassermann reaction constantly negative in serum and spinal fluid. Repeated examinations of the urine on a few occasions, only, gave weak reaction for albumin.

The course of the disease was progressive: gradually he became very stiff in the whole body, quite helpless, he could neither stand nor walk without assistance. Speech more and more affected. Steadily increasing tremor of the arms; when he was, for instance, in a sitting posture, the violent shaking of the head was transmitted all over the body. The respiration was frequently tachypneic, difficult, at night with a "cornage"-sound. Laryngoscopy, 10th of May, showed: no paresis of the soft palate which, however, is in an unceasing tremor-like

motion. No paresis of the vocal cords. The cords are in a constant vibratory motion round the middle position between abduction and adduction; he is however able to close his glottis so as to phonate, and during inspiration the vocal cords are fully abducted. No labio-glossal paresis, atrophy, or fibrillation were apparent; the above-mentioned facial paresis gradually became very doubtful (facial rigidity?).

Gradually there appeared faint, frequent, though not quite rhythmic or synchronic, medium to rapid, myocloniform jerks in the right facial region (orbicularis, cheek, angle of the mouth) and in the left side of the chin. Now and then coarse, upward jerks in the left leg.

There was still, however, no true paresis of arms or legs; brisk tendon reflexes without clonus, no definite Babinski reflex. Sensibility and sphincter functions unimpaired.

No ocular palsies, pupillary disorders or nystagmus. Eye grounds normal.

Spinal puncture 8th May 1922 showed: cells 7/3, globulin 0, albumin 12. Wassermann reactions constantly negative. On certain days there was still a trace of albuminuria. Although frequently tested, no fever observed. The pulse varied between 70 and 96, always regular. Cardiac attacks never occurred.

The patient was removed to the Municipal Almshouses where I had the opportunity of examining him a few times: his condition continually exacerbated owing to an aggravation of the afore-mentioned symptoms. Of new symptoms only more compulsory outbreaks of weeping, an inclination for grimacing, extremely difficult and almost unintelligible inarticulate speech, were evidenced. No dysmasia or dysphagia. No myotonic symptoms; a pronounced general muscular rigidity with considerable bradykinesia was apparent.

Psychically he was very bradyphrenic, though certainly not demented; his faculty for retaining freshly imparted impressions was almost unimpaired.

Fig. 9 shows the peculiar type of face with the severe grimacing during attempts at speech.

During the first phase of the disease one felt tempted to consider it as an acute nephritis with uræmic symptoms, perhaps in conjunction with a cerebral arteriosclerosis.

The later course of the disease, with its constant progressiveness, with the more and more pronounced blending of extrapyramidal (dystonic, hyperkinetic) and

“pseudo-bulbar” symptoms, the mild pleocytosis and hyperalbuminosis etc., all this taken together, justifies in my opinion, the diagnosis of “chronic epidemic encephalitis”.

Noticeable, also, are the peculiar hyperkineses of the palatal and laryngeal muscles as seen also by Lhermitte (cf. below p. 71). Stern found, in one of his patients, by laryngoscopy, a spastic contraction of the entire entrance to the larynx; Kennedy, Davis & Hyslop, mention similar findings.

2. INTERMEDIARY TYPES.

Under this heading will be grouped a number of clinical types in the symptomatology of which the extrapyramidal syndrome becomes less prominent — even though certain of its components are frequently present — while other nervous symptoms dominate the picture. The causation of these clinical types by an encephalitic infection is not so immediately obvious as it is, for instance, in the cases of parkinsonism or extrapyramidal hyperkinesia.

As will be amply illustrated by the case histories reported in the following pages, we are confronted with cases of a more or less “apoplectiform” type, for instance; or with clinical pictures suggestive of cerebral tumour or of disseminated sclerosis; or, again, resembling idiopathic affections of the spinal cord of quite a different nature, etc. In several of my cases the reader will no doubt find that the diagnosis might be open to further discussion. And, precisely for this reason, these cases are included here: for, however interesting the encephalitic extrapyramidal syndrome is in its various nuances, we shall not fully realise the terrible ravages brought about by epidemic encephalitis, unless we in time learn to diagnose these “intermediary” types of the disease, which to a

large extent contribute to the symptomatologic polymorphism of chronic encephalitic nerve diseases.

If, by way of survey, we were to enumerate all the neurological symptoms, or syndromes, which may be met with in these intermediary types, we should have to give an account of large sections of the semiology of the nervous system. I will therefore confine myself to describing some of the main features, otherwise referring to the actual cases.

In some of these cases the symptoms from the pyramidal tracts dominate the clinical picture.

We have, thus, cerebral hemiplegia, which has its onset either during the acute phase¹⁾, or shortly afterwards, passing more or less persistently into the chronic stage together with other neurological, vegetative, psychic, or similar symptoms (Cases 13, 14, 39). In other cases hemiplegia occurs as a delayed, perhaps remittent, manifestation of the chronic encephalitic cerebral changes (Cases 25, 27), or, again, it appears as a more isolated apoplectiform relapse (Case 17).

From a semiological point of view, in regard to distribution, electivity, spasticity, hyperreflexia, Babinski reflex, etc., these encephalitic cerebral cases of hemiplegia or hemiparesis resemble, in their main features, those due to other pathological causes. A concomitant apoplectiform attack with coma, etc., is however of rather rare occurrence; frequently the hemiplegia has a gradual development, sometimes segmentally. The previous history, the combination with other symptoms more peculiar to encephalitis, should help one in making the diagnosis.

The duration of the hemiplegia is extremely variable (cf. my cases). Other unilateral symptoms may coincide with the paralysis, as, for instance, tremor on the same side (Case 13), hemichorea (Case 1), etc. In Case 13 the

¹⁾ As far as the writer is aware, described for the first time by Buzzard & Greenfield (Brain 1919, vol. 43, p. 305).

hemiparesis passes more and more into a Parkinsonian syndrome. Again, the hemiplegia may disappear, while, for instance, constantly progressing psychotic symptoms, vegetative disturbances, or the like, betray the persistence in the brain of the encephalitic process.

Definite aphasic symptoms I have not seen; in Case 19 the somewhat apoplectiform disturbance of speech is no doubt a kind of dysarthria. The pronounced pathological changes found in the centres of speech in Case 59, indicate, however, that we may expect occasionally to find true aphasia also in chronic epidemic encephalitis¹⁾.

Cortical hyperkinetic phenomena, more especially in the form of epileptiform convulsions, are evidently of less frequent occurrence in chronic epidemic encephalitis than are the hyperkineses of an "extrapyramidal" origin. Jacksonian epilepsy I have seen in two patients only (Case 18, 29)²⁾. Generalised epileptic attacks are more frequently met with, either complete or incomplete (Cases 17, 22, 23, 24, 25, 28, 31, 56, 61). The tetaniform attacks in Cases 28 and 61 are no doubt either of a striatal or, at least, of an extrapyramidal origin.

Spinal syndromes of various type, parapareses, amyotrophies, sensory disorders, sphincter troubles, etc. occur as fundamental symptoms in a number of peculiar and diagnostically important cases, which will be dealt with later on (p. 124).

¹⁾ In a case of acute encephalitis in a man of 52, with epileptiform generalised convulsions, right-sided hemiplegia, pronounced somnolence, and a mild delirium, bilateral Babinski reflex, 26 mononuclear cells in the spinal fluid, blood pressure 160 mm, temperature rise to 40.4° C, there was an unintelligible paraphasia and word-deafness. Autopsy showed perivascular infiltrations in the pons and medulla oblongata, and, in the left temporal lobe a diffuse focus of confluent perivascularities with considerable necrosis. No definite arterio-sclerotic vascular changes.

²⁾ Case reported by Burger & Foequet (quoted by Mlle. Lévy).

Involvement of the cranial nerves is frequently found in chronic epidemic encephalitis, either carried over from the acute stage, or of later incidence, sometimes arising a year or more afterwards.

The ocular nerves are most frequently involved. Reys' statistics, based on the examination of 63 patients two years after the onset of the disease, afford striking evidence of this fact. It should be noticed, however, that while in some few cases the eye symptoms of the initial stage may persist during the further course of the encephalitis, they will, as a rule, disappear. And the eye troubles, setting in later, will usually present semiological features which differ rather much from the initial eye symptoms. These will usually consist of more or less isolated palsies of extrinsic eye muscles, of a nuclear origin, whereas, in the chronic stage, troubles of intrinsic eye muscles or impairment of associated movements of the eyes, i. e. supranuclear palsies, will predominate. The same patient may often present different forms of ocular involvement.

Thus, Reys, in his 63 patients, found pupillary anomalies 91 times; Pette found them in 28 of 38 patients, examined from eleven months to three years after the onset of the disease. Anisocoria is often seen, either persistent or transitory (Cases 8, 34, 42), sometimes associated with pupillary unrest (Case 2). Disturbances of the pupillary reactions should be especially sought for in chronic epidemic encephalitis, and will often be found: absence of reflex reaction to light, bilateral (Nonne); or unilateral (Moris Grossmann)¹); absolute loss of reaction to light and on accommodation (Case 6); or merely sluggishness of reaction (Case 5). Most peculiar and of a certain diagnostic value, moreover, is the isolated accommodation areflexia, the frequent occurrence of which in epidemic encephalitis

¹) Lhermitte states, curiously enough, that Argyll-Robertson's pupil does not belong to chronic encephalitis, but should always arouse the suspicion of syphilis.

has been pointed out by Wilson, Lapersonne, Hess, Dazzi, Reys (in 14 patients), and which is seen also in my Cases 4, 13, 20, as a more or less complete paralysis. Subjective impairment of vision (inability to perceive near objects, dimness of vision) frequently betrays the accommodation paresis

Westphal has described an absolute disappearance of reaction of the pupils (with mydriasis) which, in otherwise normally reacting pupils, can be elicited by pressure in the ileocecal region, by making the patient press the physician's hand vigorously, by frightening him, or some such means. It is said that this pupillary immobility can persist for about 15 minutes¹). Other authors (Nonne, Stern) have not succeeded in eliciting this phenomenon, nor have I myself.

Piltz describes an "amæboid" change of shape in the pupils, with preserved reflexes²). This phenomenon possesses scarcely any special diagnostic value; perhaps it might, like the pupillary phenomenon of Westphal, indicate a certain instability or hyperexcitability on the part of the sympathetic, oculopupillary apparatus; cf. my Case 55.

Involvement of the extrinsic eye muscles, more especially in the form of isolated ocular palsies, which are of such frequent occurrence in the acute stage, are not especially frequent or, at any rate, not especially pronounced in chronic epidemic encephalitis (Cases 9, 25, 31, 45). Such palsies of individual eye muscles do however become of great diagnostic value in cases where they represent a relapse, as for instance in Cases 33 and 64.

¹) Zeitschr. f. ges. Neur. & Psych. 1921. Vol. 68. 266. Westphal correlates this phenomenon with the pupillary immobility found in catatonic or hysterical stupor and draws attention to Bumke's mydriatic-rigid "terror pupils". The mechanism governing the phenomenon is in all probability either the evoked affective reaction or a "spreading" of a maximum muscular innervation.

²) Revue neur. 1921. p. 793.

An encephalitic woman of 31, who is at present in my department, for several years presented only general nervous symptoms (fatigue, etc.) and an increasing depression leading to an attempt at suicide. Not until some time after her admission here, did a paresis of the right abducens and the right trochlearis occur; some days later, hypesthesia and hypalgesia in the right upper trigeminal region were found, and also a right-sided corneal anesthesia, and (rare) myoclonic jerks in hands and feet. Flat temperature curve; normal humoral syndrome.

Far more characteristic of chronic epidemic encephalitis are the supranuclear pareses, the impairment of associated movements of the eyes, which are found in a more or less pronounced degree in many of our patients (Cases 5, 13, 33, 61, 62). Barré, Velter, Reys, Bollack, and others, especially call attention to the insufficiency of convergence movements, with crossed diplopia; this was found in our Cases 7, 13, 33, 61; Reys saw it in 23 of his cases. According to the above named authors it may be less a question of paresis than of hyperrigidity and motor sluggishness.

Nystagmus is not of common occurrence in chronic epidemic encephalitis¹⁾. In my opinion, at any rate, it does not occur with the same frequency, persistence, and intensity as in disseminated sclerosis²⁾.

It was almost a dogma during the first epidemic outbreaks of encephalitis, that the optic nerve was practically never involved. We have, however, had to alter our view in this respect also; even though affection of the optic nerve is far from being so frequent (more especially in the chronic form of encephalitis) as, for instance, in disseminated sclerosis, it can however occur. We may come across both an optic neuritis, a papillary

¹⁾ Still, Reys states to have observed it in 28 patients out of 63.

²⁾ The coarse unrest of the eyeballs in Case 60 is semiologically, and presumably in its patho-physiological mechanisms, essentially different from nystagmus.

stasis, a retrobulbar neuritis, and a (consecutive) atrophy of the optic discs (Hess, Cruchet, Verger & Moulinier ("forme amaurotique"), and others).

Involvement of the optic nerve was found in our Cases 13, 16, 19, 29, 30, 34, 61, with more or less pronounced defects of the visual fields. Even though, for instance, the presence of a retrobulbar neuritis would primarily suggest a disseminated sclerosis, we must not wholly disregard the possibility that chronic epidemic encephalitis now and then may occur in the form of an entirely or almost wholly monosymptomatic affection of the optic nerve. Quite recently, I examined a man of 35, in whom a bilateral retrobulbar neuritis with central colour scotoma had developed slowly in the course of three to four months, and who showed absolutely no other subjective or objective neurological symptoms than a pronounced somnolence, so that he "goes to sleep whenever he sits down on a chair".

Whether it is always the optic nerve itself and not, for instance, the chiasma, the optic tracts or the optic centres, which are involved, is difficult to ascertain (compare case 17). Stern, in one case, found perivascular infiltrations in the chiasma. In a patient with hemianopsia, and pupillary immobility, who was however not admitted to my department, the most likely supposition was that he suffered from an affection of the optic tract¹⁾.

Of the other cranial nerves, the facial nerve is most frequently involved, usually more in the form of paresis than of paralysis, partial or complete. I will not waste space on this symptom, but confine myself to remarking that it has been supposed by E. Mueller and Stiefler, that certain isolated facial palsies with an acute initial phase might be a monosymptomatic manifestation of an encephalitis infection. This possibility cannot be denied, more especially as we are, in fact, ex-

¹⁾ Arlt has recorded a case of hemianopsia.

tremely ignorant of the etiology of the ordinary rheumatic facial palsy. The hyperthermia sometimes accompanying the onset of the palsy tends to support this supposition¹⁾.

The bulbar cranial nerves may be affected, either singly, or in various combinations. Lhermitte, H. Colin, and Nicholas, found atrophy of both temporal muscles and of the left masseter²⁾, so also Krebs. An isolated involvement of the hypoglossus with atrophy of the tongue was seen in my Case 9. Sicard & Clerc, and Grossmann, have likewise described hemi-atrophy of the tongue. Difficulty in chewing and swallowing is seen in Cases 36, 46, 60. A more pronounced dysphagia is very rare. A case of Claude & Schaeffer, in which the difficulty of deglutition necessitated artificial feeding by means of a feeding-tube³⁾, stands quite by itself. Dysmasia, by itself, is far more frequent, in which case it may be a question of a co-action of paresis, hypertonia, motor sluggishness and, occasionally, involuntary muscular movements (Case 60).

Just as in regard to disturbances of speech, respiratory troubles, bradycardia and tachycardia, and the like, it is often difficult to decide in the cases of swallowing disturbances, whether it is a question of true bulbar symptoms or of a supranuclear, or perhaps, a striatal involvement. Wexberg who has given a survey of these disturbances of mastication and deglutition, considers most of these cases as having a pseudobulbar, supranuclear, or striatal origin⁴⁾. According to the pathologic findings the patho-physiological mechanisms are often perhaps mixed, bulbo-suprabulbar (cf. chapter on „Pathology“).

The respiratory disturbances constitute an interesting chapter in the semiology of chronic encephalitis.

1) Compare also a case in the paper by Jarl Hagelstam cited below. In Stiefler's one patient an abducens paresis on the same side occurred a year later.

2) *L'Encéphale* 1923 p. 85.

3) *L'Encéphale* 1923, p. 85.

4) *Zeitschr. f. ges. Neur. & Psych.* 1922 Bd. 71. p. 210.

These often have a very grotesque, "hysteriform" character; they may occur in parkinsonism as well as in the hyperkinetic or more complex types of the disease. It should be especially noticed, however, that they sometimes appear as a monosymptomatic trouble, wholly, or almost wholly constituting the symptomatic picture of a chronic epidemic encephalitis (Stern), at any rate for a time, a circumstance which does not tend to make the diagnosis easier.

The respiratory disorders have been described by Barker & Sprunt, A. J. Hall, Krambach, Hamel, Goldflam, Stern, and others, and more elaborately by French authors, Achard, Marinesco, Bériel, Laignel-Lavastine & Manigot, Vincent & Bernard, Babinski & Charpentier, and especially by Pierre Marie & Mlle Lévy¹⁾. Of Scandinavian authors, Jarl Hagelstam²⁾, Wigert, and K. Winther³⁾, have recorded some cases.

Pierre Marie and Mlle Lévy group the respiratory disorders under the following three headings: 1) True disturbances of the respiratory rhythm (polypnea, bradypnea, apnea; phasic disturbances); 2) spasmodic coughing; 3) respiratory tics, often accompanied by abnormal sensations in nose, throat or pharynx.

Polypnea is of most frequent occurrence, usually coming on in attacks, for instance towards evening, not infrequently at a more or less definite hour. The attacks last for varying periods of from less than an hour to the whole of the night. Both respiratory phases are accelerated; the authors compare this phenomenon with the well-known type of tachypnea observable in dogs when they get over-heated. In other cases the polypnea is permanent, sometimes with intervening phases of bradypnea or apnea, for instance during attempts at writing (Fig. 10). And, while the polypneic crises are usually not

¹⁾ Revue neur. 1922 p. 1233.

²⁾ Finska Läkarsällskapets Handlingar, 1923. Bd. 55 p. 69.
(Discussions of the Finnish Medical Society).

³⁾ Neurological Society of Copenhagen 2nd May 1923.

accompanied by true dyspnea, cyanosis, action of the auxiliary respiratory muscles, or by a change in the pulse rate, true pulmonary changes may sometimes be found in connection with permanent polypnea (acute emphysema, pulmonary œdema; Vincent & Benard).

Bradypnea is far more rare, being also usually phasic. In its extreme forms it develops into apnea, often, for instance, as an initial deep inspiration ("a sigh") followed by a more or less protracted respiratory pause. Or, again, slowly developing apnea may terminate in a deep inspiration and pronounced "cornage" sound. One of my patients with uncomplicated encephalitic parkinsonism had himself noticed that during work he had a tendency to "keep his breath" for about 30 seconds at a

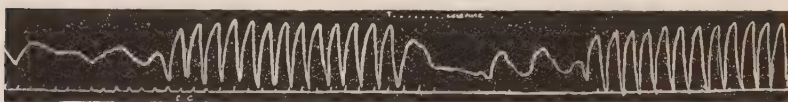


Fig. 10. — (After Mlle Lévy).

time. There is a trace of Cheyne-Stokes' type of respiration in our Case 58, otherwise it is seldom met with (Mlle Lévy).

Spasmodic coughing may likewise be the sole "sequel" to an encephalitis. It manifests itself as a dry, reiterated, "little cough", without wheezing respiration, and, like the polypnea, is usually confined to definite hours, towards evening, etc. The attacks may become extremely violent, ending in vomiting, involuntary micturition, and so on. In some patients this spasmodic cough may persist all through the day, not even ceasing during sleep.

The respiratory tics manifest themselves now as constant sniffing, hawking and spitting, now as more polymorphous, often very noisy puffing or hissing or snorting, through the nose or through the mouth. These respiratory disorders also occur, as a rule, in phases, or

like true paroxysms, during which the patient "stands immovable, with eyes shut, absolutely indifferent to everything around him, panting incessantly until he collapses" (Mlle Lévy).

The two latter forms of respiratory disturbances seem to occur mostly in children, where they often run parallel with psychic disorders, especially with a more or less pronounced emotional erethism, so as to form one of the components of the psychomotor instability which often characterises these little encephalitic patients.

The peculiar grotesque pictures afforded by these respiratory disorders, their coincidence with psychotic, general nervous, "hysteriform" or "neurastheniform" troubles, their being "punctual to the hour", their liability to being influenced by psychic factors, and, finally, their frequent monosymptomatic appearance, at any rate for a time, all these features may delude one into conceiving them as purely hysterical. Semiologically, too, they often show a considerable resemblance to the respiratory disturbances found in true hysteria. A psychogenic blending cannot, of course, be totally disregarded, especially in as much as the initial and purely organogenic attack may, during its further development, become tainted by reactive anxiety symptoms.

Respiratory troubles were found also in my patients, usually, however, of a somewhat more moderate and transitory kind: serial yawning or sighing (Case 8), sighing respiration or hiccoughing, with or without abdominal myoclonia (Case 41), awakening with polypnea, and "being out of breath", as if the patient had "run upstairs to the fourth floor" (Case 55). In case 4, the bradypnea was periodically very pronounced. In case 11, in which the tachypneic attacks came on during the night, with "cornage sound", a laryngoscopic examination revealed a tremor of the soft palate and the vocal cords¹). In the

¹) Lhermitte has also described continuous tremor of the soft palate and the vocal cords in a patient with a striatal syndrome.

patient mentioned as case 46, the respiratory disturbances (tachypnea, arthymia) accompanied the exacerbations of muscular unrest. Also at times when there were no actual attacks — and when the respiratory type was not changed to any essential degree — the stethoscopic examination revealed a markedly saccadé respiration, suggesting a diaphragmatic spasm, or the like, as demonstrated by means of the radiogram by Vincent & Benard, and Laignel-Lavastine & Maginot, in their cases.

A small girl under my observation, who did not show any other morbid signs than disorders of sleep, had a respiratory tic consisting in a persisting blowing upon her fingers, as though they were numbed by cold.

Case 12, a girl of 18 years, admitted to my department November 28th 1923, and who is still under my care¹⁾, shows respiratory troubles of a more peculiar kind, for a time manifesting themselves mostly as paroxysmal yawning, as described in the cases of Sicard & Paraf, Mayer and de Saussure, and as mentioned also in my cases 7 and 10.

Gradually, her yawning tics changed into most pronounced paroxysms of polypnea.

Case 12. She had "Spanish disease" in 1920, had to stay in bed for 3 weeks, with considerable rise of temperature, somnolence, no eye symptoms. After that time, she suffered now and then from giddiness, headaches, swoons of short duration, slight pollakuria, some polydipsia, no menstrual troubles. About a year ago, she had, for some weeks, fits of hicoughing, each of a few minutes' duration. From January 1923, she has had her "yawning-tics". Without visible external cause and without having been subject to emotion, she is suddenly seized with 4 or 5 clonic, quick jerks in the muscles of the neck, so that her head is bent backwards and a little to the left; at the same time, but not quite synchronously, the mouth is opened through similar yawning-jerks, accompanied by short, staccato inspirations; sometimes, as also seen in the ward, there are twitchings round the mouth and slight clonic jerks in the left shoulder

¹⁾ Demonstrated in the Neurological Society of Copenhagen, March 26th, 1924.

During the fits, the face is slightly flushed; no true dyspnea or polypnea, nor any change of rate or regularity of pulse. Clouding or loss of consciousness was never noticed, nor tongue biting or involuntary micturition¹). The fits occur rather frequently, up to 20 times a day; also a few nocturnal fits, during her sleep. After the jerks have ceased, she feels rather "sore" in the epigastric region. A systematic testing of the functions of the stomach revealed nothing abnormal. Nor did a thorough neurological examination give any definite pathological symptoms. Examination of the cerebro-spinal fluid yielded 2/3 cells, 0 globulins, 10 albumins, the Wassermann test being negative here as well as in the blood. With the increasing frequency of the fits, the temperature, which had hitherto been normal, shows a rising tendency, some evenings to 38.4; the pulse rate sometimes will leap up to 110.

She is a little psycho-infantile; no pronounced emotional erethism, no hysteric stigmata.

During her later stay in the ward, her fits have become excessively frequent, up to 135 a day, having, too, changed as to their character: The head is still agitated by strong clonic jerks, but the mouth is kept wide open during the attack, (which may last up to a minute) while there is a continuous polypnea (up to 70 respirations per minute), rather rhythmic and very noisy.

Another interesting point in this case is the paroxysmal hiccupping of a year ago.

It would be reasonable to anticipate that the paroxysmal hiccup might occur more or less as an isolated symptom in chronic epidemic encephalitis. Such cases have also been reported by Popper and Logre, Henyer & Bourgeois²). In Denmark, Dr. Axel V. Neel, assistant pathologist to the Psychiatric Laboratory, has recently examined this question. His investigations showed that our first cases of epidemic hiccup were reported in December 1920, that is to say, about a year after the first reports of cases of epidemic encephalitis. Since then, 565 cases of epidemic hiccup have been reported, while the reported cases of epidemic encephalitis have been far less numerous (compare the curve in Fig. 11).

¹) For many years, she has suffered from nocturnal enuresis.

²) *Revue Neur.* 1922, p. 1509.

The epidemic hiccough would then seem to come dragging after, in localities in which outbreaks of epidemic encephalitis have already occurred. An enquiry limited to the small island of Bornholm, where Dr. Neel has personally been able to investigate 12 cases, may prove of interest. In one case hiccoughing set in with other, lethargic symptoms; in the remainder of the cases there were no such initial symptoms. Of these patients one had had a typical lethargica a couple of years previously; in nine patients other neurological symptoms were discovered, such as diminished reaction to light of the pupils (5 times), absolute immobility of pupils (once),

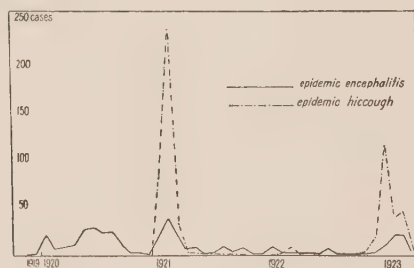


Fig. 11. — (After Dr. Neel).

unilateral ptosis (once), diplopia (twice), impairment of convergence-movements of the eyes (4 times). The hiccough-paroxysms lasted for $11\frac{1}{2}$ to 10 days, day and night, were very violent, loud and noisy. Finally, it is worth mentioning that the epidemic hiccough attacks men to an overwhelming degree (93 % men to 7 % women).¹⁾

Disturbances of speech, apart from the bradyphasia of parkinsonism, are to be found in many of

¹⁾ A more complete record of Dr. Neel's investigations will be published in *Revue neurologique*. These investigations seem decidedly to contradict the view advanced by Sicard that the epidemic hiccoughing should be considered not as a simple ("monosymptomatic") form of encephalitis, but as being due to a "co-virus"; Lhermitte, Bing & Staehelin go in for the identity.

our patients, more or less pronounced and persevering (Cases 19, 36, 43, 44, 45, 46, 59—61). Sometimes the bulbar-dysarthric, and sometimes the pseudobulbar-spastic characteristics are the more prominent: blurred, nasal, lisping, strained, breathless, stuttering, staccato speech, explosive falsetto voice, etc. True scanning of speech is very rare; literal ataxia, as in general paresis, I have not observed. In some cases the disturbance of speech was noticeably progressive, ending in anarthria.

Cerebellar symptoms have been described by Chalié, Barré & Reys, Bonhoffer, Bostroem, Hegesy, and others. In a few of my patients, also, I have seen symptoms that may be, wholly or partly, of a cerebellar origin, for instance vertigo, certain disturbances of gait (Case 28), etc. One might also be justified in searching for a cerebellar component in so far as action tremor, and static tremor are concerned, perhaps also in certain forms of "torsion spasm" and the like. It is striking, however, that a systematic examination of the cerebellar functions ad modum Babinski practically never reveals typical disorders of these functions. Now and again, in isolated instances, adiadokokinesis appears (Cases 13, 60, 62), although even this is probably, in parkinsonian patients, only a pseudo-adiadokokinesis, due to the rigidity and the bradykinesia.

Investigation of the vestibular functions shows in most patients normal conditions. But the possibility of a predominant "labyrinthine" type of chronic epidemic encephalitis (Barré & Reys) ought most certainly to be born in mind.

Sensory disorders, subjective and objective, have been reported by Pierre Marie, Souques, Sicard, d'Achard, Léri, Holthusen & Hofmann, Stern, Mlle Lévy, Sauer, Stertz¹⁾, and others. It is reasonable to assume that, in the course of time, "sensitive" types of chronic epidemic encephalitis will prove to be by no means rare.

¹⁾ Klin. Wochenschr. 1923. p. 1063.

In addition to the above-mentioned pains in parkinsonism, we often observe pains which either precede or accompany certain hyperkinetic types (Case 41), in these cases being not infrequently localised in that extremity or that portion of the body in which the hyperkinesis later sets in. Sometimes the pains have a "myalgic" character, sometimes a "neuralgic" one, occasionally, tenderness of the muscles and nerves to pressure is found. In one of my patients (Case 53), these pains came in attacks, though only when she was at rest, while they disappeared after a brief period of work, or by walking, as was also the case with Sauer's patient.

Now and again these pains are accompanied by painful paresthesia¹). Isolated fits of hemi-paresthesias are seen in my Case 40, in which also appeared hemiparesthesias of smell and taste.

The localisation of these pains is very varying: — the trigeminal region (Cases 8, 39, 55); the neck — face — shoulder region (Case 28); a cervico — brachio — intercostal localisation (Sicard); or, again, resembling sciatica, as in one of my patients. Finally, the picture may certainly, in some cases, become that of a multiple neuritis (Stern's case 3).

Objective disorders of sensibility are not altogether of infrequent occurrence; they have, for example, been described by Mlle Lévy, Sauer²), Stern, and others, and were seen for instance in my Cases 8, 38, 39, 54, 55. Most often it is only a question of hyperalgesia, or hyperesthesia; but, at other times, we get a more or less complete abolition of the various components of cutaneous sensibility, while the deep sensibility remains unaltered. The topography of the troubles is sometimes peripheral, sometimes radicular or segmental, spinal or

¹) Thus, one of my patients complained of an extraordinary sensation of cold in the left shoulder and arm, that is to say, in the areas in which parkinsonian symptoms soon after appeared.

²) *Zeitschr. f. ges. Neur. & Psych.* 1922. Bd. 79, p. 589.

cerebral, though often with an irregular distribution. Pathological alterations have been found in different parts of the sensitive tracts. In the purely clinical cases it is often very difficult definitely to ascertain the site of the lesion.

The diagnosis of that type of chronic epidemic encephalitis possessing a predominant sensitive ("algic") character, as for example an isolated trigeminal neuralgia (Léri), will not infrequently cause difficulty, more particularly when other encephalitic symptoms are lacking. In one of my cases frequent (subfebrile) rises of temperature occurred during the whole course of the disease¹). From the point of view of differential diagnosis it is most certainly of importance to remember the possibility of such predominant neuralgic or neuritic forms of chronic epidemic encephalitis: Stern mentions a patient who was for quite a considerable period wrongly treated for coxitis; pseudo-appendicitic pains, perhaps as prodromes for abdominal myoclonia, have also been described, and have, at any rate in one case, misled to an operation (Schaller & Olliver; compare Case 45).

Mlle Lévy mentions more especially joint affections, consisting in pains, redness, slight swelling, mostly of larger joints and most frequently monarticular, preceding, for instance, a myoclonia localized to the extremity concerned.

Yet we may certainly in some cases come across a polyarticular picture, that may be mistaken for a case of true rheumatic fever until more conspicuous nervous symptoms will appear, as may be learnt from my cases 35, 45, and 64.

In the last patient a radiogram revealed later on a most marked osseous atrophy in the affected wrist. Reys mentions a possible occurrence of a myositis ossificans in parkinsonism. And K. Petré, of Sweden, has described a case of encephalitis with peculiar osseous neoformations

¹) In two of Stertz's cases similar conditions were found; in his third case there was almost complete "profound areflexia".

on the surfaces of the femur and the humerus, analogous with the para-osteo-arthropathy which has been observed by Mme. Dejerine & Ceillier in severe cases of paraplegia.

In intermediary types as in parkinsonism, a more or less conspicuous component of abnormal muscular movements often enters, i. e. an extrapyramidal hyperkinesia of various kinds. I think it however most practical to describe these peculiar motor disturbances in connection with the clinical pictures in the symptomatology of which they constitute the dominating feature.

The first of my "intermediary" cases forms a natural transition to the Parkinsonian group inasmuch as the original cerebral-hemiplegic condition is gradually absorbed in a dystonic-bradykinetic syndrome.

Case 13. Male, aged 17, son of a workman, for the first time admitted to my department 13th August 1920. Previously he had, on the whole, been healthy; had never had any nervous attacks. He was a lively, intelligent boy of good character.

In July 1920, typical encephalitis lethargica: fever, somnolence, at times delirious, restless; singing, hallucinations, etc. No convulsions, pareses of the eye muscles, or the like.

When brought here, 13th August 1920, he was still decidedly somnolent, and continued thus for about 3 months, after which period he gradually passed into a state of moderate bradyphrenia. No facial or ocular paresis, but bilateral optic neuritis, with respectively 3 and 2 diopters' swelling of the discs, and rather marked exudation. The temperature rose slightly at the beginning, up to 38.3 in the evening; some tachycardia. The urine was free from albumin and sugar. Spinal puncture showed: cells 36/3, globulins 2, albumins 10—15; Wassermann reaction in serum and spinal fluid negative.

Six days after his admission to the hospital a paresis of the left arm developed rather rapidly, and a few days later, a paresis of the left leg. The paresis was flaccid, with slight ankle clonus, no definite Babinski reflex; no disturbances of sensibility.

A more constant Babinski reflex in the left foot now appeared; the patient's gait was impaired, there was spastic carrying of the left leg, combined with a cerebellar component of reeling and swaying.

At the same time he grew more and more obese, with abdomens pendens. The genitals were well developed, but not remarkably big; scanty pubes. No swelling of the thyreoid gland. X-raying of the cranium revealed no enlargement of the sella turcica. Psychically he was at this time no longer lethargic, but distinctly bradyphrenic, dull, revealing reactions only at the sight of food. The hemi-paresis persisted unchanged until his discharge 13th January 1921. He had steadily gained in weight, from 35 to 52 kgs (height 163 cm.).



Fig. 12.

He was readmitted 26th April 1922, with the diagnosis of "dementia præcox". From a neurologico-psychical point of view his condition had remained almost unchanged, except that he had become more "rigid". He was very sluggish both in speech and motor reactions, his speech was bradyphasic, with a slightly nasal tone. Pronounced bradykinesia; he took an "eternity" to dress, eat, etc., etc. General bearing rather Parkinsonian. Very slight traces of beard; average growth of axillary hair, vigorous pubes; genitals well developed. He had become even more obese than formerly.

Examination of the eyes now revealed abolition of convergence movements, restricted lateral and upward movements, while the downward movements were normal. The outlines of the optic discs were still indistinct; the fields of vision was

normal. The pupils were equal in size, the reaction to light well preserved, the reaction on accommodation however diminished (6 diopters in both eyes against 15 normally).

There was only a suspicion of paresis in the left arm, while the paresis of the left leg was rather pronounced; no marked hemirigidity, only a faint indication of tremor. Gait the same as during his previous stay. Lumbar puncture showed: cells 3/3, globulins 0, albumins 10; Wassermann reaction constantly negative.

He was removed to the Municipal Almshouse 23d June 1922. On the 18th May 1923 however, he had to be readmitted to my

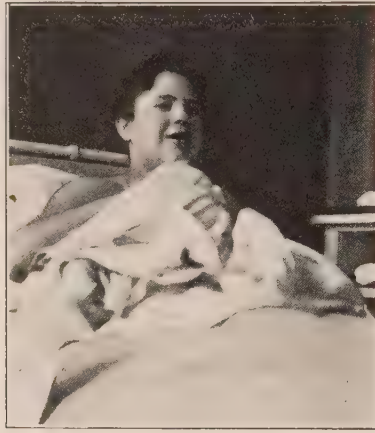


Fig. 13.

department: His "silliness" had gradually become more pronounced, he became more and more apathetic and uncleanly, smearing excreta and urine about, and he had developed a propensity to tease, proving on the whole disagreeable to those around him.

This time he was extraordinarily obese, weight kgs. 68.8. His face is generally quite immobile, though it may at any moment be drawn into a stereotyped broad grin (Fig. 12). Now and then explosive laughter sounding something like 4 to 5 hiccupping chuckles. Marked bradyphasia; on one occasion he was mute for 4 days. Pronounced bradykinesia, extremely slow in eating, dressing, lapses into reveries, often with the arms in catatonoid positions (Fig. 13), or he keeps standing in statue-like attitudes, etc.

Slight impairment of convergence movements. Pupils equal in size, reaction to light preserved, reaction on accommodation absent. Eye grounds normal(?).

He still has a slight leftsided hemiparesis with definite Babinski reflex, but without rigidity. On the whole, there is more frequently a slight hypotonia in the muscles of the extremities and of the trunk. No myoclonic muscular reaction. No tremor, myoclonia, abnormal synkineses, or the like.

When standing or walking he pitches his body very much backward, without simultaneous flexion in the knees. This back-



Fig. 14.

ward-pitching movement is more especially noticeable when he stands erect (Fig. 14). The "opisthotonus" is not spastic, it can easily be corrected passively. He walks with excessive slowness and gravity, with a flaccid carrying forward of the legs; with traces of circumduction of the left leg and a drooping of the forefoot. Marked retropulsion and slight anteropulsion; no true cerebellar reeling, no cerebellar asynergies nor any pronounced dysmetria revealed by other tests. No ataxia of arms or legs; adiodokokinesis (pseudo-adiodokokinesis?) on both sides. No disturbances of sensibility or sphincter control.

He states himself that he is able to run better than to walk, which also proves to be the case.

During his entire stay his temperature has been normal; periodically pronounced tachycardia; the diuresis strikingly reduced. The urine was free from pathological substances. He is an ortho-regulator. Blood pressure 110 mm.

Quite recently he was attacked by motor inertia in the W. C., the door of which he had bolted; he sat there for from 3 to 4 hours. When someone knocked at the door it was evident that he tried to unlock it; this effort, however, only resulted in his sticking firmly to the bolt and lying with the whole weight of his body against the door. A man had therefore to enter through the window to rescue him. After this he was practically mute for some days, he could only with difficulty utter single words; when he was interrogated, he seemed to stop short completely, with open mouth and a hopelessly inane grin.

Repeated examination of the eyes on the 1st November 1923 revealed complete convergence paresis; strabismus alternans; diplopia cannot be evoked. The pupils react well to light. Ophthalmoscopic inspection showed that the discs are somewhat pale, without swelling, though however with somewhat indistinct outlines on the nasal side. Visual acuity on both sides $<5/12$. Visual fields normal, no colour scotoma; i. e. there is now a slight secondary atrophy of the optic nerves.

On January 21, 1924 he was transferred to the asylum for insane, "St. Hans", at Roskilde. There, his condition grew rapidly worse, he became strongly somnolent and bradyphrenic, quite inert, with difficulties of swallowing. A pneumonia set in, and he died January, 30th, 1924. The post mortem findings will be reported in the chapter on pathology (p. 280).

Case 14. Concerns the afore-mentioned boy with *pubertas præcox*, aged 11 at his first admittance to my department on the 19th October 1920. Previously healthy, with a normal, physiological development, without nervous attacks, a clever and intelligent boy, he was taken ill with a typical encephalitis lethargica in the beginning of August 1920, with fever, somnolence, ocular symptoms (ptosis, squinting, anisocoria, accommodation paresis), Spinal puncture showed: cells 5/3, globulins 1, albumins 15. In the 5th—5th week of the disease a leftsided hemiplegia gradually developed, with rigidity, tremor of left limbs, hyperreflexia profunda, but no Babinski reflex. At the same time there was slight bradyphasia and bradykinesia, spasmodic weeping and laughter.

On his admittance here there were still rather pronounced residua of the neurological troubles. The temperature was normal; rather noticeable tachycardia. Psychically his state was somewhat remarkable: undisciplined, interfering, laughing and chattering,

with a tendency to automutilations, scratching himself all over the body, biting of nails, incessant sucking of fingers, etc.. Night-sleep somewhat disturbed. After a month's stay he was taken home by his parents, and was again admitted on the 12th October 1921. At school he had only been able to hold his own because he was shown special indulgence, his memory for fresh impressions had proved to be very defective, he could not take in what he was reading and exhibited no interest in it. He flew readily into a passion, constantly had rows with his



Fig. 15.

school-fellows. He had developed a tendency to lie, had become mythomaniac, boasting, very obstinate. His sleep continued to be bad. He was very sluggish at everything, ages over dressing, and the like. The hemiparesis varied somewhat, being most pronounced in the morning, on the whole he dragged very much on his left leg, in such a way that "the heel of his boot was as flat as the sole".

His total appearance and behaviour were on the whole more or less the same as during his first stay, his general temper fluctuated somewhat, mostly he was flippant, wild, sometimes obscene. He was soon taken home again by his mother, but was readmitted 3d March 1922, because he had been somewhat agi-

tated at home, with hypnagogic hallucinations for a fortnight or so. In the ward he was clear and had no hallucinations. The hemiparesis was about the same; fine static tremor in the left arm. He was removed to the Municipal Almshouses, from whence he returned home in September 1922, and was admitted for the fourth time to my department 6th January 1923.

He had constantly suffered from sleep disturbances, always finding it difficult to fall asleep; added to this, nocturnal states of agitation had developed: he awoke between 3 and 4 in the morning, tossed about in his bed, lashed himself on the thighs, called his parents, ran about in the rooms, etc., went to sleep again after a lapse of 3 til 4 hours, and then slept soundly until late in the afternoon the following day. He was also very restless, very irritable, teasing, and mischievous, in the day-time. His general temper fluctuated, somewhat "sentimental", mostly, however, merry, singing, chattering, meddlesome. He still had bad habits, such as biting his fingers until they bled, snapping with his fingers, and the like. Intellectually he was very childish, "like his brother, of eight years".

He has recently begun to be importunate towards girls, he embraces, kisses, and caresses them; no more serious attempts, however; masturbation has not been observed.

In the ward, too, he was somewhat silly, but he submitted to the rules of the house; at times he was a little impertinent; however he displayed no coarser erotomania here.

His general appearance was rather childish; weight kgs. 50.1; not specially obese. His voice was in the breaking stage. Growth of hair on the upper lip; axillary growth of hair absent; pubes very abundant. Penis excessively big, testes also big (1 to 2 cm), cf. Fig. 15.

A pronounced hemiparesis persisted with some rigidity. No parkinsonism, no tremor, no myoclonia. The temperature was normal, as was also the urine. He showed dysregulatio ammoniacae. He was removed to the lunatic asylum (St. Hans Hospital).

The cases of the following series are all held together by the decided phasic development of the clinical picture, until the almost apoplectiform onset of the symptoms, etc.¹⁾.

¹⁾ Sicard (in *Le Journal médical français* 1923, t. XII p. 111) describes 3 cases which evidently correspond with mine. He calls them "mésocéphalites à rechute" (and discriminates them from the encephalitis s. s.; cf. p. 302).

Case 15. Male, aged 21, admitted 14th February 1923. Since his 8th year he has suffered from an ear trouble. Three years ago, he had the "Spanish disease"; he lay in bed, however, only one day, his temperature was about 38° , no definite drowsiness, no eye symptoms. Subsequently he suffered a good deal from headaches, sensations of fatigue, and giddiness, but no vomiting or endolic phenomena. He had no swoons or convulsions; never subjective febrilla. There were no ear symptoms (increased otorrhea, pains, or the like).

On the evening previous to his admittance he had a violent headache, he took a few headache powders (no hypnotics, etc.). In the morning of the day of his admittance he still felt very unwell, he swayed when he got up, fell at last to the ground and lay in a coma for about 6 hours. During this time there were no convulsions, nor any other form of muscular unrest, no involuntary micturition, no vomiting. When he awoke at last, he felt pretty well, his headache having abated considerably.

On admittance he was clear-headed, completely orientated; the reactions were lively. Speech natural. No paresis of the eye muscles, no nystagmus; the pupils were equal in size and reacted well, the reaction on accommodation being perhaps a little impaired. Eye grounds, fields and acuity of vision were normal.

No stiffness of the neck; Kernig's sign absent. No paresis of face or of limbs. No hypertonia or sluggishness of movement. No tremor nor any other muscular unrest. The tendon reflexes were normal, the plantar response on the left side, however, showed a slight tendency to be of the extensor type. His gait was normal, except now and then for a slight suggestion of reeling.

The examination of the fauces, the thoracic and abdominal organs revealed absolutely nothing abnormal. Blood pressure 100 mm. The pulse rate was normal and regular during the whole of his stay. The urine was free from albumin, blood and sugar. Hg (Sahli) 78 %. Spinal puncture showed: cells 68, globulins 0, albumins 15; the Wassermann reaction in serum and spinal fluid was negative.

The temperature on the evening of his admittance was 38° , later it was normal.

During the remainder of his stay until the 10th March 1923 he felt perfectly well, he only remained at the hospital on account of the examination of the acid regulation which proved him to be an ortho-regulator.

The otologic examination, which was of particularly great interest in this case on account of the previous

history, produced a slight, foul-smelling secretion in the right tympanic cavity, the walls of which were covered with polypous granulations; the tympanic membrane was very defective. The mastoidal region was normal on both sides; nothing abnormal in the left ear. He heard whispering at a distance of 0.20. No spontaneous nystagmus. The conclusion arrived at by the otologist was: as there is no pain in the right ear, no increased otorrhea, nor right-sided headache, an otogenic, endocranial affection (*abscessus cerebri*) is not likely.

The course which the illness took neither corresponded with the usual endocranial ear complications; nor were there found others of the more usual etiological factors which might explain the appearance of this apoplectiform and so speedily vanishing clinical picture, which was accompanied by a slight rise of temperature and strikingly marked lymphocytic pleocytosis in the spinal fluid (and slight hyperalbuminosis). I think that these two factors indicate that we have to deal with an infectious noxa. And I do not think that we can here dismiss the association with the "Spanish disease" of three years ago, howsoever mild the attack appeared to be; the headache, the lassitude, the dizziness, also form a chronological and clinical link between this febrile phase and the present attack.

We may give a similar explanation of the following Case 16, here, however, with greater certitude.

Case 16. Male, aged 46. Previously healthy. In November 1921 he was taken ill with fever (up to 39°), headache, perspiration, but did not go to bed. After about a week, the fever subsided, being followed by a clouding of vision (not diplopia), and the patient was admitted to the Hospital for epidemic diseases 16th December 1921. He was subfebrile, very drowsy, with headache and dimness of vision. The examination of the eyes revealed a pronounced optic neuritis. There was no stiffness of the neck, nor any trace of Kernig's sign., no paresis of eye muscles or of the limbs, no involuntary muscular unrest. Hyper-reflexia was found with a trace of ankle clonus, on the left side; no Babinski reflex. The spinal puncture gave clear fluid

at increased pressure; cells 310/3 (lymphocytes), globulins 10, albumins 30—40. Wassermann reaction negative in both serum and spinal fluid.

All the symptoms vanished, and the patient felt perfectly well at his discharge, 4th January 1922; subsequently he was in good health, able to work until the 20th September 1922 when, in the morning, he suddenly felt giddy, he swayed, could not turn the leaves in his books, and his speech became "thick". This attack lasted about 1 1/2 hours. After that he felt tired, he went home after 3—4 hours, noticing now that he was dragging his left leg and that his left hand moved awkwardly, "he pulled everything down", etc. No loss of consciousness, no dysphagia.

He was admitted to my department 25th September 1922. He was a man of robust appearance, not presenile. The radial arteries not rigid. Blood pressure 120 mm. Pupils equal in size, reacting to light and on accommodation. No pareses of the eye muscles, except that the left eye, at convergence movements, quickly becomes tired and deviates to the left. No diplopia. No nystagmus. Eye grounds, acuity of vision, visual fields, normal.

His speech is unimpaired. No facial or lingual paresis. Slight paresis of the left arm, most pronounced in the extensors (fingers, wrist, elbow) and in the adductors of the shoulder. In the left leg only, some weakening of power in the extensors of the foot-joint and the toes. No pronounced hypertonia. The tendon reflexes of the left side are a little more brisk than those of the right, but there is no clonus. Indication of Babinski response on the left side. No sensory disturbances. No tremor at rest, but in the left arm there is a slight swaying during voluntary movements. No abnormal involuntary movements (myoclonic or the like).

Spinal puncture: clear fluid; cells 5/3, globulins 0, albumins 10; Wassermann reaction negative in serum and spinal fluid.

Stethoscopy of lungs and heart showed normal conditions. The urine was free from albumin and sugar. Hæmoglobin 75 %. The temperature was normal during the whole stay; pulse rate 76—92 a minute, regular.

Apart from some headache the day after the spinal puncture there were no general cerebral symptoms; psychically he was quite natural.

On his discharge, 25th October 1922, there were no nervous disorders except for a slight sensation of heaviness in the left arm and a little dragging of the left leg.

I do not think there can be any doubt that the initial febrile state of the patient has been an epidemic encephalitis with a somewhat protracted course; the clinical symptoms as well as the pronounced humoral syndrome confirm this hypothesis.

Our examination in the ward gave no points of support of the assumption of another etiology for the hemiparesis, which appeared about a year later, more especially as nothing was found indicating syphilis, pre-senile arteriosclerosis, tumor cerebri, etc. And this transient hemiplegia also corresponds very well with the symptoms observed in other cases of chronic epidemic encephalitis, such as reported below. It may be that these apoplectiform relapses are especially due to the vascular changes occurring in chronic encephalitis, small hemorrhages, thrombosis, or, more rarely, meningeal hemorrhages (case 65).

Case 17. In the following case, there can be no doubt as to the nature of the nervous disease. The patient was a male, aged 27, who was admitted to my department October 16th, 1923. He had suffered from a somewhat indefinite "Spanish disease" 4 years previously, with little fever and no cerebral signs; the illness had persisted for some weeks. He then enjoyed excellent health until the day before his admittance, when he complained of headache, vomited, became a little delirious and, finally, had an epileptiform seizure with stiffening of the limbs, trismus, froth round the mouth, loss of consciousness, subsequent amnesia.

In the ward, he was rather somnolent, not quite orientated. The speech was slightly blurred. A pronounced left-sided hemiplegia of arm and leg was discovered; facial paresis was doubtful. Tendon reflexes were slightly increased on the left side, on which a marked Babinski reflex was also found. An almost complete analgesia and anæsthesia were found over the left arm and leg, and the left half of the trunk. Left abdominal and cremasteric reflexes were absent. Only on the first day of his stay some few myoclonic twitches in left arm and leg could be seen.

There was no difficulty of swallowing; type of respiration normal. Pupils equal in size, the left reacting rather sluggishly to light. He could not read the letters on the test card (paralysis

of accommodation). Fields of vision could not be examined owing to his mental condition. No pathologic changes of the eye grounds. No impairment of movements of the eyes; no insufficiency of convergence movements.

In the spinal fluid were found 64 cells, small lymphocytes and large mononuclears together with a number of polynuclears. The figures for the globulins and the albumins were 0 and 14, respectively. Wassermann reaction negative in blood and spinal fluid, as was also the Sigma reaction. No bacterias were

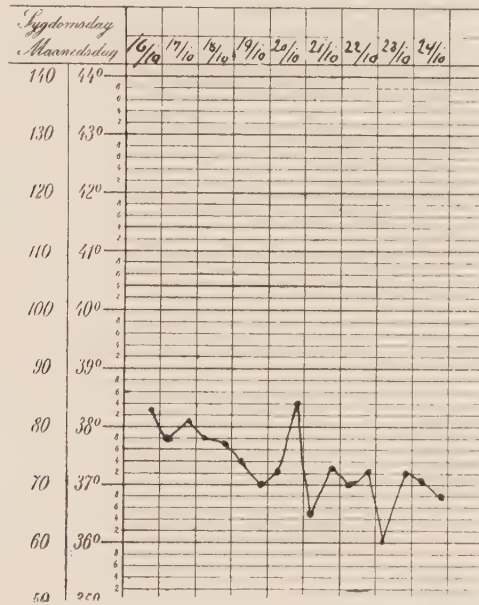


Fig. 16.

found in the spinal fluid. His temperature was somewhat elevated for a few days (Fig. 16), rate of pulse rather varying, with a marked tendency to bradycardia. No pathological findings in the ears, the heart, the lungs, or in the urine

After about a week, he was almost clear of mind. The hemiplegia had also subsided. There was now a fairly marked ataxia of left arm and leg. Impairment of the cutaneous sensibility persisted, while he also showed loss of "joint-sense" as well as astereognosis in left hand. He still complained of "blurred sight", became giddy, when rising from his bed, and suffered from headaches now and again. A renewed spinal puncture on

the 10th December 1923 yielded cells 13/3 (lymphocytes), globulins 0, albumins 9, the Wassermann test in blood and spinal fluid being still negative.

He was given an argotropine treatment, the temperature during this treatment rising a little, up to 37.9° and continuing thus, with slight increases in the evenings for about a week after the last injection of argotropine. His hemiplegia continued to improve, and he could get out of bed and walk about, though with a rather marked hemiplegic gait. Apart from a rather pronounced impairment of memory for newly imparted impressions, he revealed no mental troubles; there was no marked

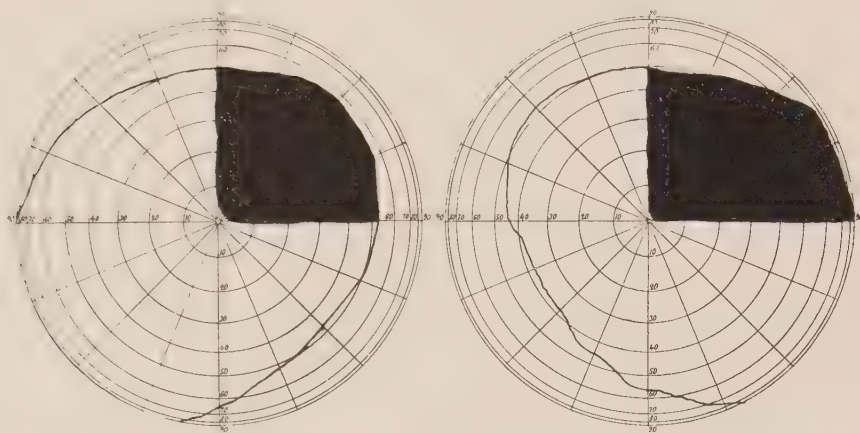


Fig. 17.

bradyphrenia¹⁾. In February 1924, on account of his persistent complaint of impairment of sight, he was once more submitted to a close ophthalmoscopic examination. The movements of the eyes were normal. Left pupil showed a decidedly weakened reaction to light as well as on accommodation. The optic discs were quite normal. Acuity of vision 5/6 in both eyes. Examination of the visual fields now revealed a homonymous, rightsided quadrangular hemianopia for testing with white objects and a total colour blindness, in both eyes, supposed to be congenital (Fig. 17).

In this patient, we have a partially febrile relapse, initiated by an epileptiform seizure, followed by hemiplegia and hemianæsthesia. Seeing that no certain involvement of the face was

¹⁾ As to his peculiar memory troubles, when he got home, compare p. 12.

found, neither motor nor sensory, one might suppose the unilateral symptoms to be depending on encephalitic changes in the pons or ponto-bulbar region. In this way, the left-sided ataxia, which developed later, would be understood, as also the slight impairment of the pupillary reactions of the left eye to light and on accommodation. The right-sided homonymous hemianopsia must have its own lesions, localised, probably, to the right optic tract or to a higher level of the optic pathway.

Especially where such apoplectiform, paretic attacks appear together with hyperkinetic symptoms, and where it is a question of comparatively younger men without cardiac, vascular or renal disease, without syphilitic infection or chronic alcoholism, and the neurological examination of whom reveals no signs of any solid (localised) process in the central nervous system (tumor, or the like), especially in such cases is it inevitable that we think of chronic epidemic encephalitis, even though, in the anamnesis, we have only information of an "influenza or the like, without any features of a "lethargica", nay, even where such information is totally lacking. Therefore, I do not hesitate to include the following case in my description.

Case 18. Workman, aged 39, admitted to my department 26th September 1922. He has been addicted to the consumption of great quantities of alcoholic drink. Sixteen or seventeen years ago he had a left-sided otitis media with radical operation of the ear and subsequent complete left-sided deafness and left-sided facial paralysis. No ear troubles subsequently. Fourteen years ago he got a fragment of glass into his left eye, blinding it.

Eighteen months ago he had the "Spanish disease": fever up to a little above 38° , drowsiness, dizziness, "the eyes would sometimes draw to the right"; no diplopia; no disorders of speech. He was ill about a week. Later he had occasional attacks of giddiness, during which everything blackened before his eyes; there was neither loss of consciousness nor convulsions.

At the beginning of September 1922 he suddenly became unwell again, he was drowsy, felt feverish. Suddenly there occurred a complete failure of speech, "he could not utter a word", The attack abated gradually in the course of an hour. The next day he suddenly got violent twitchings in the

right side of the mouth and tongue, the latter "curling itself up" toward the right; the attack lasted a few minute, without clouding of consciousness, leaving a slight paresis of the right angle of the mouth. During the following days there ensued similar short attacks of facial spasms. At the same time he suffered from pains in the forehead and increased attacks of giddiness. On the day previous to his admittance to the hospital one of the above mentioned attacks of facial spasms occurred, this time, however, the twilchings spreading to the right arm, the legs not being affected. There was no loss of consciousness, biting of the tongue, or involuntary micturition.

He is of good physique, not presenile, without radial arteriosclerosis, blood pressure 120 mm.

On admittance his temperature was 37.9°, pulse rate 72, rhythm regular.

On the left eye coloboma of iris with uveal prolapse, resorbed lens, choroidal atrophy; he can only just perceive the hand moving before the eye. The right eye showed normal pupillary reactions, normal visual acuity and normal eye grounds. The movements of the eyes were unimpaired; no nystagmus.

Left-sided, peripheral, though not complete, facial paralysis. Slight paresis of lower parts of right facial nerve. Slight clonic jerks of the left facial muscles. No glosso-labial atrophy or fibrillation; the tongue deviates a little towards the right on protrusion. Movements of the palate free. No disorders of speech except a little "jerkiness" now and then (labial fibrillation?).

The muscular strength in both arms was somewhat diminished, almost equally, on the two sides; in the legs it was unimpaired. No hypertonia. Tendon reflexes brisk without clonus, no Babinski response. His gait was very vertiginous-reeling (without, however, any definite direction of falling); there was noticeable swaying when in the erect posture.

Fine shaking of the right arm on the finger-to-nose-test, coarse oscillation of the left leg on the heel-to-knee-test (not quite so pronounced in the right leg). No muscular unrest in the extremities when in a resting position; nowhere any myoclonic jerks.

The examination of the ears showed nothing abnormal excepting the usual defects following upon a radical operation, in the left ear, "especially nothing which might point to intracranial complications".

X-raying of the cranium: no signs of brain tumor.

Spinal puncture: Fluid clear Cells 3/3 (1 lymphocyte, 2 somewhat larger, mononuclear cells); globulins 0, albumins 10; Wassermann reaction in spinal fluid and serum negative.

The urine was free from albumin and sugar. The temperature was normal during his further stay in the hospital.

In the beginning he suffered very much from headaches and dizziness; he had rather frequent attacks: He turns giddy, feels sick, perspires freely, has coarse arrhythmical spasms in the right half of the face spreading to the right arm and the right leg, whereas there are no spasms in the left limbs. These attacks remind one of very pronounced shivering fits. Before and after them his temperature was normal. There was never any loss of consciousness, biting of the tongue, or involuntary micturition. The attack would last a couple of minutes. No postparoxysmal pareses.

The patient's condition improved considerably after he had been treated with cacodyl; his gait grew natural, the aforementioned attacks became rare, though the facial spasms and the action tremor remained almost unchanged.

Spinal puncture carried out on the 10th January 1923 showed: pressure 165 mm, cells 8/3 (7 small and one big mononuclear lymphocyte), globulins 0, albumins 10—11.

He was discharged a week later, and commenced work; he continued however to have tics in the left half of the face, also tremor, especially in the right arm, and occasionally a marked dizziness. In the month of May he still had some of his "shaking fits". Now and then headaches without vomiting, at times sleeplessness; but no diurnal attacks of somnolence, or subjective febrilia; there was some emaciation.

On the 16th October 1923 he was again admitted to my department. During the last month he had become more sluggish and "apathetic", he could not attend to his work, and the day before his admittance to the hospital he was again seized with cloniform spasms in the right side of the face and in the right arm, of a few minutes' duration. There was no loss of consciousness, however, or biting of the tongue; these fits eventually occurred so frequently that there were practically no intervals, and during this "status epilepticus" there was on one occasion involuntary micturition. During one of these fits the left arm is said to have become stiff in an extended posture, (the right arm being at the same time slightly flexed), but without cloniform jerks. There were no spasms in the legs. The patient was himself able to describe his seizures: the head and eyes were turned upwards toward the right, "his tongue worked round in the mouth, he knew perfectly well what he wished to say, but could not utter a single word. At times his teeth were clinched very tightly together".

On admission he still lay in a fit; perfectly conscious, he could speak and give the above information, but his speech was difficult, broken, and not distinctly articulated. The respiration was slightly polypneic, syncopated, somewhat strained, but there was no cyanosis. Pulse about 80, regular and strong; temperature 38°.

The right side of the mouth was somewhat flaccid. No paresis of the limbs; the patellar reflexes were lively, without clonus; no Babinski response; the pupils reacted well.

During the following night he had several fits, after which they ceased. He was not unconscious during the attacks which began in the region of the right eye and right angle of the mouth, and then spread to the right arm, but never to the left arm or to the legs.

After that his condition was practically the same as during his first stay: tic-like jerks in the left facial region, alternating, not rhythmical, without contracture of that half of the face; tics were never observed in the right half of the face. The right side of the mouth a little flaccid. No paresis of the tongue, no labial nor lingual atrophy or fibrillation, no definite tremor in arms or legs, the strength and tonus of which were not distinctly changed. When walking there was some tilting towards the left side.

No difficulties of swallowing or mastication. The pupillary reaction and visual acuity were normal in the right eye; there was no pupillary stasis. The examination of the ears gave the same results as during his previous stay.

Spinal puncture: cells 43, globulins 0, albumins 7. Wassermann reactions in serum and spinal fluid were negative. The temperature was normal except on the evening of his admittance to the department. The urine was free from pathological substances.

Psychically he was on the whole normal. Neither lethargy nor mental sluggishness were evident.

To sum up, his condition was at first suggestive of an otogenic cerebral affection, even though the ear disease had begun sixteen or seventeen years ago and had apparently been cured as a result of the radical operation to which it had been subjected. In the opinion of the otologists it appeared most unlikely that an otogenic brain disease existed. Moreover, the other more usual causes of cerebral troubles (such as arteriosclerosis, syphilis, brain tumor) could be excluded. There were neither

cardiac nor renal affections, and it would be extremely difficult to associate these peculiar cerebral attacks with the patient's abuse of alcohol. On the other hand, the picture may be readily understood as being due to a chronic epidemic encephalitis.

The following case will probably appear even more disputable in regard to its diagnosis as chronic encephalitis. But for this very reason it has been included here, because it has been the experience in my hospital, particularly in these peculiar cases where the diagnosis is doubtful, that as one of the possibilities a polymorphous chronic encephalitis should not be disregarded.

Case 19. Farmer, aged 42, single, admitted 5th February 1923. In 1895 he had "pneumonia", without cerebral symptoms. No definite rheumatic fever.

In 1912 "Spanish disease", i. e. fever up to 40°, headache, "he slept all the time", or was delirious, he had twitchings in arms and legs, could not speak ("unable to utter a single word"). Half a year later he still had frequent "jerks" in his back, so that "he was quite bent double".

He was then in good health until August 1922, when he had to stay in bed for some days suffering from pronounced giddiness and drowsiness, to such an extent that he had to be roused for meals; he had difficulties of speech (his voice was thick, he could not articulate a word); his temperature was not taken.

Subsequently he recovered. Then, on the 5th February 1923, after getting up, he again felt very unwell, with pains in the forehead, dizziness, dimness of vision; he was unable to stand erect, and felt by turns hot and cold ("shivering fits").

On admittance here he was febrile (39.6°), very drowsy and indolent; his speech was thick, nasal, he had difficulty in articulating words; he also spoke very slowly. All his movements were bradykinetic, fumbling, and his hands shook and trembled when he touched anything.

There was lessened action of the left angle of the mouth: the tip of the tongue deviated a little towards the right. There was neither atrophy nor fibrillation of lips or tongue. No difficulties of mastication or swallowing; no distinct paresis of the palate.

The eye movements were free; no nystagmus. The left pupil was wider than the right one, with diminished reactions on

accommodation; the reactions of both eyes to light very lively. The ophthalmoscopy showed normal conditions.

No pareses of the limbs; no rigidity; tendon reflexes fairly brisk without clonus; pronounced Babinski response on the left side. No disturbances of sensibility, noticeably not in the face. No myoclonia.

Nothing in the fauces; no herpes labialis; nothing abnormal in the lungs. With regard to the stethoscopic examination of the heart see below. Blood pressure 110 mm. Pulse 88, regular, vigorous. The urine was free from albumin and sugar. Weight 76 kgs.

Spinal puncture on the 7th February 1923 showed: cells $\frac{1}{3}$ (big mononuclears), globulins 0, albumins 8. Wassermann reaction negative in both serum and spinal fluid.

On the day after his admittance his temperature was still $39,2^{\circ}$ in the morning, $37,8^{\circ}$ in the evening; afterwards it remained normal. On the 2nd day after his admittance an improvement, already became noticeable in regard to his drowsiness, his unsteadiness of movements, and his disorder of speech. In the course of a further few days his apathy had disappeared, his mind was clear, and he was steady in his movements, suffered but little from headache. He still showed a somewhat stooping carriage, his face was very stiff, his gait a trifle slow, there was, however, no pronounced rigidity, nor any pronounced general bradykinesia; the facial paresis was just perceptible, the Babinski reflex very doubtful; the speech a little bradyphasic and dull. The spinal puncture on the 3d March 1923 showed $\frac{7}{3}$ cells, globulins 0, albumins 13; the Wassermann reaction was constantly negative in both serum and spinal fluid.

On isolated occasions during his further stay a slight bradycardia was observed. Stethoscopy revealed the heart dullness to be normal, function regular, no pulse deficit, no accentuation of the second pulmonary sound, no murmurs, except over an area of about the size of a florin at the level of the apex-beat, where pleural (pericardial?) friction sounds were heard in systole, less frequently in diastole.

Thus there is most likely a question of limited pleural or pericardial thickening which may probably be due to his pneumonia attack of 1895, while an endocardial affection may presumably be excluded. We may also exclude the interpretation of the patient's acute bulbar syndrome as being caused, for instance, by embolic processes, an interpretation, moreover, which is also con-

tradicted by the rise of temperature, the marked somnolence, etc.

According to the history of this case, the type and grouping of the symptoms, the lack of other etiological clues, the diagnosis of "epidemic encephalitis" appears to me also here to be the most likely one (compare also the attacks in Case 16). We find in this patient also the febrile relapse which figures in some others of my cases. When, on the 31st March 1923 the patient left my department, a developing parkinsonism was strongly suspected.

At present we are completely ignorant as to how long the encephalitis virus may remain virulent in the human organism, and we are, therefore, as yet unable to tell at what exact moment the infection has taken place in our patient: in 1912 he suffered from an infectious disease which bore a most marked resemblance to epidemic encephalitis, with a febrile-lethargic-myoclonic picture, with disorders of speech, and finally with myoclonic jerks in the back lasting half a year subsequently. Has he been well since then? Is he cured of the infection, and does the attack in August 1922 denote a reinfection? These are questions which it is at present impossible to answer with anything like certainty; however, they will later be the subject of further consideration (p. 302).

On p. 22 I have mentioned lethargic attacks as symptoms of epidemic encephalitis, and I have also stated that this paroxysmal shifting of consciousness might occur in connection with more complicated pictures such as "somnambulism", nocturnal "dreamy states", etc. Lethargic attacks have been described by Babinski & Charpentier among others¹⁾, noctambulic and somnambulic attacks by Progulsky & Grober²⁾, and by H. Colin³⁾. In

¹⁾ *Revue neur.* 1922 p. 1369.

²⁾ *Münch. med. Wochenschr.* 1921.

³⁾ *Annales med.-psych.* 1923, an. 81. 86 (homicidal impulses during somnambulism).

cases where such attacks occur without being combined with other neurological symptoms of a more conspicuous organic nature¹⁾, or where the attack, by its features, has on the whole a somewhat "hysteriform" character, as in one of the cases reported below, there is a great risk of mistaking them for hysteria.

Case 20. Male, smith by occupation, aged 37, married, at the department from 24th January 1923 to 4th February 1923.

The patient had the "Spanish disease" in February 1920, i. e. fever up to 40, pronounced somnolence, some clouding of consciousness; no definite eye symptoms or myoclonia. Subsequently he has suffered from dyssomnia, general fatigue, attacks of dizziness with vomiting and fine tremor of both hands. In addition he has suffered from headaches — slight attacks which gradually became more persistent, and then more pronounced attacks occurring at intervals of days or weeks: after a couple of days the headache gives way to extreme drowsiness accompanied by incessant yawning which lasts up to 12 hours.

Now and then visual disturbances of short duration occur, so that he cannot read his newspaper. Neither convulsions nor pareses, difficulties of speech or of swallowing were observed.

About a week before his admittance to the department he had fever up to 39°, violent headache, drowsiness and visual impairment.

On admittance he looked healthy, he was psychically clear, not drowsy. The pupillary reactions and the eye grounds were normal; there was neither paresis of the eye muscles nor nystagmus; the fields of vision were normal.

There were no pareses of the cranial nerves or of the limbs, no rigidity and no indications of parkinsonism. The tendon reflexes were normal; there was no Babinski response. Neither tremor nor myoclonia. No sensory disturbances.

The temperature was 37,9 on the evening of admittance; the pulse 60, regular and strong. Stethoscopy of heart and

¹⁾ In one of my patients, a somewhat imbecile girl, aged 18, the lethargic attacks only occurred about four years after the febrile initial phase. Episodical rises of temperature, transitory insufficiency of convergence movements of eyes and abolition of accommodation assured the diagnosis. The humoral syndrome was normal.

lungs showed normal conditions. Blood pressure 110 mm. The urine was free from albumin, sugar and urobilin.

Spinal puncture: cells 2/3 (lymphocytes), globulins 0, albumins 11; Wassermann reaction negative in both serum and spinal fluid.

During the rest of the patient's stay at the hospital, until February 4th 1923, the temperature remained normal except for a few evenings when it rose to 37.8. None of the attacks described were observed. The pulse rate oscillated between 60 and 80. On his discharge he felt perfectly well.

In this case, other more usual symptoms of chronic encephalitis are so pronounced that the character of the "lethargic" attacks is quite obvious. In fact, the attacks with the headache, drowsiness and yawning, the rise of temperature and the characteristic visual disorders, undoubtedly indicate slight relapses of that "lethargy" to which the disease owes its first name.

In the following patient the troubles of consciousness display a more polymorphous picture. Frequently the attacks consist of a narcoleptic phase of short duration, which may be closely followed by a somnolent-delirious phase; at other times we get attacks with a more "hysteriform" muscular unrest.

This patient also presents a series of other characteristic encephalitic symptoms, in rather close chronological connection with the infectious initial stage.

Case 21. Pharmacist, married, aged 36, at my department 8th to 27th March 1923.

Gloomy, sensitive nature; good faculties. In 1910 he had diphtheria with pareses of arms and legs and difficulties of swallowing; he recovered only after the lapse of about a year. In 1916 precipitation accompanied by fainting, however without definite subsequent cerebral symptoms.

In August 1918 "Spanish disease", the temperature rose to 40.2, headache, dizziness, diplopia, but no muscular unrest. He did not stay in bed, but attended to his work, notwithstanding the hyperthermia, etc., lasting for about four weeks.

The fatigue, headache, dizziness, frequently associated with a reeling gait and stumbling, persisted. Towards the end of the year 1918 he used to get "sleeping fits", especially when he

was very tired, and principally in the evening: he would suddenly fall asleep, dropping whatever he carried in his hands, his eyes would close and he would not react when spoken to. This phase lasted at most for only a few minutes whereupon he would waken up, though most frequently only to pass into a sleep-like state of a couple of hours' duration, during which he would snore, talk in his sleep (about the occurrences of the day, or the like), accompanied by violent jerking of the muscles of the body, especially in the legs and neck. After that he would again awaken, feeling comparatively well. Following on these attacks his speech was frequently "thick" for a period of up to several hours; there was neither paresis of the limbs nor any distinct aphasic disturbances. Involuntary micturition was never observed during the attacks.

Gradually he grew slower of perception, with some failure of memory, on the whole he became more "drowsy" in his manners. Now and then he had attacks of dyspnea with palpitations and anxiety. At his work in the chemist's shop he gradually became very much troubled by the unsteadiness of his hands, "he groped two inches to the right of objects he desired to get hold of". Now and then diplopia and squinting were experienced.

His psychic indolence etc., his reeling gait, the "groping" movements of his hands, led at last to his dismissal, a fact which was partly contributed to by his being suspected, quite erroneously, of abuse of morphine and alcohol!

In 1921—1922 he was for some months treated with hectin injections at Dr. Neel's private clinic, and improved somewhat. Dr. Neel has kindly put his journal at my disposal. Among other symptoms he found slightly clouded discs, the right knee jerk absent, doubtful left-sided Babinski reflex, slight ataxy on the finger-to-nose test. The spinal puncture showed $\frac{4}{3}$ cells, globulins 0, albumins 20. — During his illness the patient has emaciated a good deal (lost about 10 kgs).

On his admittance to my department he was in a decidedly somnolent state; when he was asked questions his answers were exceedingly indolent and given in a half annoyed manner; it was evident that he had to "hunt" for them; at any moment he would fall into deeper somnolence, from which he could however be roused for a short while. He was not really confused when one succeeded in rousing him.

He was pale, sallow, complained of pains in the neck. Neither vomiting nor signs of meningitis were noted.

The face was strikingly immobile, the play of the features reduced to a minimum; when showing his teeth there was labial tremor. The eye movements were free, there was no nystagmus.

Eye grounds, acuity of vision and fields of vision, were normal. The pupillary reactions to light and on accommodation were well preserved.

His speech was somewhat slow, monotonous, there was however no true dysarthria. No difficulty of swallowing, nor dysmasia.

No pareses of face, tongue or limbs. No pronounced bradykinesia nor hypertonia. Arm reflexes normal. The knee jerks can only be elicited by means of Jendrassik's manœuvre; the Achilles jerks are absent. Left plantar reflex frequently a rapid dorsal flexion of the big toe, the right of the flexor type. When standing erect his head stoops slightly; the attitude of his body, however, is not typically Parkinsonian; he walks somewhat slowly, taking rather short steps; there is a strong swaying of the body when undergoing Romberg's test.

No tremor or muscular unrest of any other kind.

The otologic examination revealed nothing abnormal on the caloric; rotatory and pointing tests; his hearing was unimpaired.

His temperature and pulse rate were normal, as were also his lungs and heart. The diuresis was strikingly reduced (340—860 ccm). The urine was free from albumin and sugar. Spinal puncture: cells 3/3 (small lymphocytes), globulins 0, albumins 11; Wassermann reaction negative in serum and spinal fluid.

The examination for acid regulation showed that he was a dysregulator.

He cleared up rather speedily, for some days however continuing to be somewhat sluggish and dysphorically sulky. In the ward, he had a few attacks, one of which was nocturnal, lasting about half an hour; he tossed about in his bed, beat with his arms, kicked; no agitation of facial muscles appeared. The expression of his face was hazy, his look confused; now and then he cried out: "Rouse me, rouse me!" The colour of his face was normal, there was no perspiration, nor froth at the mouth, no disturbances of respiration nor biting of the tongue or involuntary micturition. After the gradual cessation of the attack he fell into natural sleep. Regarding this attack the patient declares amnesia.

One day, just after a visit of his wife (the visit having been somewhat short in his opinion) he got a slighter attack with kicking in bed etc., which the nurse declared to have appeared more like a "fit of anger", and which lasted about 5 minutes; of this attack he also declared that he remembered nothing whatever.

He subsequently grew rapidly quite normal psychically, he had no further attacks, and was discharged feeling perfectly well.

In this case the diagnosis "chronic encephalitis" evidently requires no further confirmation in regard to the complete clinical picture. Only with reference to certain of the attacks, more especially the diurnal one here at the department, a slightly functional blending might perhaps suggest itself, as indeed such could be expected beforehand in this as in other organic cerebral troubles. The majority of the patient's attacks however appear to me, in accordance with their total aspect, truly organic; though, of course, it is not unlikely that the patient's inherent nervous temperament may be able to "emerge" during these organic attacks and, to a certain degree, give the muscular disorder that emotionally expressive, "hysterical" character.

A similar psychogenic blending may possibly be traced in the attacks of the following patient.

Case 22. Shop-girl, aged 17, admitted 20th January 1923. Intellectual faculties and habitual temper of average type. As a child she walked in her sleep, otherwise there were previously neither definite nervous nor psychotic disorders. Menstruation regular from the age of 15; no parturition or miscarriage.

In 1920 "Spanish disease" (the whole family was taken ill), she was very ill, lay in bed for 3 weeks, fever up to 40°, very marked somnolence, violent "trembling" of arms and legs, no true convulsions or eye symptoms of any kind.

After the illness she was somewhat more indolent, she would sit about listlessly, partly erethic, with globulus, palpitations, crying fits; she slept badly.

One day in the middle of 1921 she suddenly got a "black spot" before the right eye, for a moment she could not see at all with it. She had similar attacks, each of a minute's duration, in the ensuing period; in the last months of 1921 she "could not see at all "with the right eye, she "had to turn her head, when she wished to see any thing to the right of her".

January-March 1922 she was in the IInd department of the Municipal Hospital. Examination of the eyes then showed: Visual acuity of right eye = finger counting at 1 meter's

distance; of left eye = $\frac{5}{6}$ (emmetropy): The right pupil was wider than the left, both pupils reacted to light and on accommodation. Atrophy of the right optic nerve. The examination of the visual field revealed similar conditions as in the later examination (cf. below; however, the sector like defect was somewhat larger). X-raying of the cranium (frontal, sagittal plans) showed no symptoms of tumor nor deformation of the sella turcica. Wassermann reaction in serum and spinal fluid was negative. The temperature, pulse rate and urine, were normal. Hæmoglobin (Sahli) 75 %. The neurological examination revealed no definite abnormal signs.

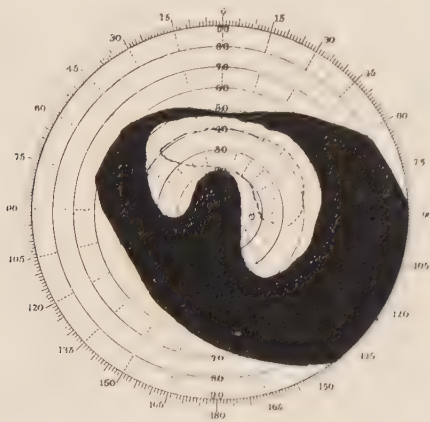


Fig. 18.

Subsequently she began to suffer from headaches, and, in August 1922, she had frequent attacks beginning with a "stitch" in the heart; she fell and lost consciousness, was at first "stiff" all over the body; this was succeeded by twitching of the head; the attack finished in a phase of slumber. The total duration of the attack was from two to five minutes. There was no biting of the tongue nor involuntary micturition; no post-epileptic confusion. After the attacks she sometimes felt a craving for air and a feeling of oppression.

More recently these attacks have been rather frequent, sometimes in short spells of 3—4; she will wake up between the attacks. Nocturnal attacks were rare. She declares that she does not remember anything about these attacks.

Menstruation regular; she has not become particularly obese; no loss of hair. No subjective febrilia.

In the ward she was lively, on the whole there was nothing psychotic, nor any emotional outbursts.

The examination of the eyes showed defects in the visual field of the right eye (Fig. 18); in the left eye the visual field was normal for white, moderate, concentric narrowing for red and green. Atrophy of the right optic nerve. The right pupil more dilated than the left, both reacting to light and on accommodation. Visual acuity the same as at the examination in 1922. No pareses of the eye muscles, no nystagmus.

No pareses of the cranial nerves or of the limbs. No hyper-tonia, nor abnormal reflexes or disturbances of the sensibility. Gait normal. Romberg's test negative. Slight static trembling of the fingers of the right hand, slight action-tremor in the left leg.

She looks healthy, is not particularly obese (weight 55 kgs). No morphologic signs of endocrine disorders; exterior sexual features quite normal. Temperature, pulse rate normal. Urine free from albumin and sugar. Blood sugar 0,074—0,072. The examination of the neutrality regulation showed dys-regulation. X-raying of the cranium: normal conditions. Spinal puncture: cells 8/3, globulins 0, albumins 8. Wassermann reaction in serum and spinal fluid negative.

During the first period of her stay in the ward she had rather numerous attacks, mostly of short duration, about half a minute, with closed eyes, apparently complete unconsciousness and absence of reaction to external stimuli, somewhat slow lateral torsion or more rapid "tossing" of the head, slight tremor of the muscles of the mouth, no movements of arms or legs. Normal colour of face. No involuntary micturition or biting of the tongue. After the attacks she at once regains her mental clarity and declares that she remembers nothing of what has occurred.

Enuresis nocturna, or sleep-walking, was not observed here.

After about five or six weeks the attacks ceased entirely, and, except for a little headache and the slight static tremor in the right hand, there was nothing particularly noticeable about her. In the middle of March she was sent home, but was again admitted a week later: At home she had been indolent and irritable by turns, she had had several attacks, had also "run away" from home a few times, on one occasion for a whole night and had afterwards been unwilling (or unable?) to give any information as to where she had been.

The father who, perhaps, treats her a little harshly, thinks that she has been with a lover she has had for some time. The father is also very sceptical about her attacks, because

they stop promptly on application of a hard brush to the softer parts of her body (!). Considering the short duration of the attacks on the whole, a fact which has also been observed here, one can scarcely attach much importance to the father's observations, in regard to differential diagnosis.

During the whole course of the disease the attacks have presented a very uniform aspect, quite without that polymorphism of movements, leading up to "*attitudes passionnelles*", belonging to the psychogenetic convulsive attack of but a little more pronounced character. Thus, after her readmittance she has had attacks commencing with tachypnea of brief duration, thereupon sudden loss of consciousness with closed eyes, bluish lips, the tongue protruding between the teeth, blue and "swollen", clonic chewing jerks of the under-jaw, rhythmic flexor-extensor jerks in the basal joints of the lightly stretched fingers, otherwise no jerks. The attacks lasted scarcely one half minute, ceasing somewhat abruptly; there was no postparoxysmal confusion. No biting of the tongue nor involuntary micturition. She herself had amnesia for these attacks.

Neither in these nor in her previous attacks of a similar kind is there anything which does not justify the interpretation of the attacks as being the result of an organic disease, i. e. of a chronic epidemic encephalitis, for which also the slight static tremor in the right hand, the slight ataxia in the left leg, but above all, the ocular symptoms, are parallel manifestations. Whether or no there is at the same time a psychogenic component in the picture, is as difficult to decide in regard to this as to the preceding case. Attention is drawn, however, to the „hysteriform taint” which also characterised the attacks of the patient in Case 61, where the organic cerebral affection was established by means of an autopsy.

Case 23. It is a peculiar coincidence that quite recently, I have got another female, aged 22, admitted to the department, with symptoms reminding one very much of those of the preceding case. She has previously been healthy, and it is particularly to be noted that she has had no hysterical or epileptic attacks. "Spanish disease" 3 years ago, without pronounced cerebral signs. Subsequently disorders of sleep, emaciation, loss of hair. Shortly after the febrile phase she began to suffer

from absences commencing with flushing. Recently she has had attacks of a somewhat different nature: palpitations, craving for air, pronounced flushing of the face, followed by excessive pallor, smacking of the lips, now and then she utters a single word before losing consciousness. No actual collapsing to the ground. The attacks are quite momentary. No biting of the tongue or involuntary micturition. The objective examination showed nothing distinctly abnormal. Nothing hysterical in her behaviour. She was a dys-regulator.

More pronounced epileptic seizures, occurring during the more acute phase of the encephalitis or during its chronic course, have been described by Cruchet, Guillain, Bauer & Hedinger, Price, Stern, Grosmann, and others. In three of my cases (Cases 28, 56, 61) there occur epileptic attacks together with other more dominating symptoms. In the following patients epileptic fits were the principal symptoms.

One of these patients was a younger man who stayed only a very short time in the department, and in whose past history there were no epileptic attacks of any kind, no alcoholism, no syphilis, nor trauma capitis, and who had neither cardiac nor renal troubles. Two years after a somewhat vague "influenza" in 1918, he suffered from typically epileptic convulsive attacks at intervals of several months. Examination showed absolutely no symptoms of any more definite cerebral trouble, particularly no indication of tumor. The findings in the spinal fluid were normal, the Wassermann reaction in serum and spinal fluid negative.

In a case like this and, until further proofs are adduced, the infectious origin of the epilepsy may of course be refuted in favour of the more generally accepted conception of a "spontaneous" outburst of a hitherto latent hereditary disposition. My other experiences in regard to convulsive attacks in chronic encephalitis have however made me doubt that this interpretation is always the correct one. In any case, such an interpretation seems to me to be very wide of the mark in regard to the following patient.

Case 24. Male, aged 16.; admitted 3d January 1923. No epileptic disposition, no former epileptic manifestations. Average intelligence.

In 1919 "Spanish disease" (the whole family was affected), high fever, epistaxis, no particular drowsiness, no muscular unrest, especially no convulsive attacks. He afterwards remained in comparatively good health for about eighteen months, when he began to suffer from nocturnal fits: without awaking he begins to kick and toss about, whereupon his whole body

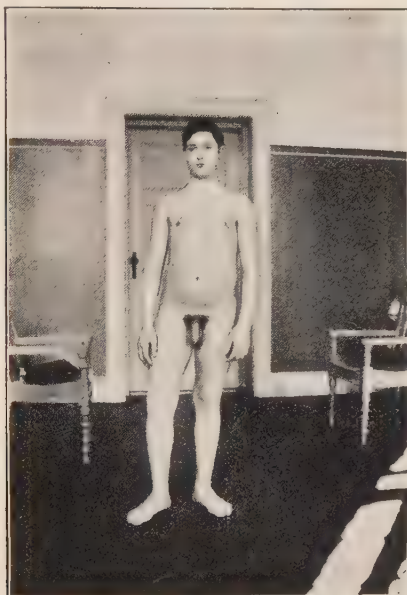


Fig. 19.

stiffens, he becomes cyanotic, he froths at the mouth, bites his tongue, and involuntarily passes urine. Subsequently he continues to sleep, snoring heavily. These attacks became more frequent, now occurring in the day-time also, sometimes as many as five or six times a day. He has, moreover, not infrequent fits of somnambulism, lasting for twenty minutes or so, during which he walks about the room, prepares sandwiches, juggles with knives, tries to get out of the window, passes urine on the floor, and offers resistance when one tries to put him into bed; yet he does not waken. Not infrequently, an epileptic seizure occurs from one to two hours afterwards. He professes

absolute oblivion both as regards the convulsions and the somnambulism.

Since the advent of these attacks, the patient has been sluggish and, possibly pre-epileptic, sulky.

He is strongly built, of healthy complexion, rather obese, he has increased in weight at the hospital, from 63 to 70 kgs (height 168 cm.). His bodily development is otherwise harmonious; there is no genital hypoplasia nor obliteration of the secondary sexual features. (Fig. 19).

Nothing abnormal in lungs or heart. Urine free from albumin, sugar and urobilin. Blood sugar 0,076—0,076. The examination of neutrality regulation shows dys-regulation.

The systematic neurological examination shows nothing abnormal beyond rather small pupillary reactions on accommodation. Spinal puncture: cells 4/3, globulins 0, albumins 8. Wassermann tests negative.

His intellectual faculties are somewhat limited, his faculty of retaining freshly imparted impressions (Ranschburg's word-pair method) good.

In the ward he had several nocturnal convulsive attacks of an epileptic nature, of short duration, with involuntary micturition. On one night he suffered from somnambulism, he stepped across his neighbour's bed, wanted to pass his urine into the urinal, but passed it on the floor. When a fellow-patient tried to awaken him, he got into his bed and kicked him out of it. On being put into his own bed again he did not waken. Upon inquiry the next morning he declared that he knew nothing about the happenings of the night.

A psychogenic component cannot be excluded in this patient either: His somnambulism is of so lengthy a duration and so polymorphous that it reminds one of hysterical somnambulism. But the apparently perfect unconsciousness and, more especially, the not infrequent termination of the somnambulism by a true epileptic seizure, seems to me to make an organic origin extremely probable. That he suffers from genuine epileptic attacks of an organic origin seems indeed to be obvious.

The patient is a dys-regulator. According to Bisgaard's and Nørvig's views this should mean that he is a "latent epileptic". This possibility cannot, of course, be excluded in regard to our patient. However, having regard to what

has been already stated (p. 30) concerning the dys-regulation, it will be easily understood that I might just as well consider the patient's dys-regulation as being acquired, and, being an encephalitic symptom (dependent on endocrinal troubles?), to be paralleled with his tendency to obesity. It is well known that French authors, Pierre Marie, for instance, have long ago assumed an infectious etiology for certain forms of epilepsy, a supposition which, even when making due allowance for the most decidedly important hereditary factors, is plausible in those cases of epilepsy occurring at a later period of the patient's life, and where no other obvious provocative causes, such as alcohol, trauma, syphilis, arteriosclerosis, nephrosclerosis, or the like, can be found.

This supposition as to the encephalitic origin of certain epileptic fits is confirmed by the following case in which other disseminated cerebral symptoms afterwards occurred.

Case 25. Male, aged 25, admitted to my department 24th September 1923. No previous epileptic fits of any kind. In 1918 "Spanish disease", i. e. fever, somnolence, perspiration, dizziness, eight days in bed.

Following on this he says that he enjoyed good health except for some fatigue until the spring 1922, when with a week's interval, he had two epileptic seizures beginning with the appearance of a "star-shaped figure" in his field of vision, followed by complete loss of consciousness, falling to the ground, tonic-clonic convulsions, cyanosis, dilation of the pupils, biting of the tongue, no involuntary micturition; these fits lasted a few minutes, and were followed by a coma of half an hour's and four hours' duration, respectively. The patient remembered nothing of his attacks. The fits were not followed by either pareses or confusion.

During the ensuing period he felt rather tired, emaciation began to take place; he did not, however, suffer much from headaches; no subjective febrilia, no myoclonic attacks, no eye symptoms.

Since September 1923 increasing drowsiness has been evidenced, impeding his work, he could sleep eighteen hours of the twenty-four. About a fortnight before his admittance he noticed some heaviness in the left arm and leg, gradually.

increasing and, in the course of a few days, developing into a moderately pronounced left-sided hemiparesis. At about the same time his eyes became "dull", he could not distinguish clearly, saw indistinctly and dimly. No convulsions or sensory disturbances, no incontinence of urine. His morning temperature was 37.5° at the highest, his evening temperature was unfortunately not taken while he was at home.

In the ward he has been rather somnolent, he has himself the feeling that he goes to sleep as soon as he lies down; when he is roused, his mind is clear and he is perfectly orientated regarding his surroundings etc. No headache, dizziness, or vomiting; he is cleanly.

The left pupil is more dilated than the right, both reacting to light and on accommodation. The field of vision is normal for movements of the hands; no colour scotoma. Ophthalmoscopic examination revealed a slight hypermetropia, the vessels of the eye grounds being a little tortuous, otherwise nothing abnormal. The eyes cannot move to the full extent in the lateral direction; no impairment of convergence movements.

The movements of the left angle of the mouth slightly impaired, both in voluntary movements and when patient smiles; frontal muscles unimpaired. The tongue deviates slightly towards the left, and fibrillates strongly. There is no marked paresis of the soft palate. No disorders of speech. No paresis of the cervical muscles. The muscle tone is reduced in the left arm, the power of which is somewhat diminished; there is an indication of ataxia in the left arm, light adiodokokinesia and dysmetria, no tremor in the arm at rest, nor static trembling.

The muscle tone in the left leg is normal, the strength of the limb being considerably reduced; no ataxy or tremor, slight bradykinesia.

The tendon reflexes of the arms feeble, the left knee-jerk and Achilles-jerk more pronounced than those on the right side, Babinski response on the left side.

No paresis of the abdominal muscles, abdominal reflexes pronounced. Nowhere any sensory disorders.

Spinal puncture: cells 160/3 (88 small, 72 large lymphocytes), globulins 0, albumins 22, Wassermann test negative in serum and spinal fluid.

The urine was free from pathological substances, both chemically and microscopically. No respiratory disorders; stethoscopy of lungs normal. The temperature somewhat varying, but he has all the time had an ulcerous stomatitis and, a few days after his admittance, he got a phlebitis in one leg, with rather high fever.

He remained somewhat somnolent, even after the phlebitis had vanished; the hemiparesis continued almost unchanged. About a month after his admittance there occurred a right-sided oculomotor paresis in the course of a day, with ptosis, the right pupil three to four times as dilated as the left, diminished movements of the eyes inward, upward and downward. The pupillary reaction to light was preserved on the first day, the reactions however being greatly diminished, and ultimately, the reaction to light completely disappeared, while the left eye continued to react promptly. No paresis of other cranial nerves.

No rise of temperature. Spinal puncture about a week later showed: 34 cells (small lymphocytes), large mononuclears), globulins 1 (?), albumins 12; the Wassermann test negative in the blood and the spinal fluid.

He was then submitted to a treatment with argotropin. In December 1923 a slowly progressing amelioration became evident. In January 1924, there remained a slight ptosis and movement of right eye impairment of inward (paresis of inferior oblique). Pupillary reactions, eye grounds normal. Vision in both eyes 5/6. His hemiparesis, too, improved considerably, so that he can now move about with a stick, although with a rather spatic gait.

I should think that the diagnosis of this case is pretty certain. In fact, the clinical picture is quite typical of the phasic and disseminated development of chronic epidemic encephalitis: An interval of nearly four years between his "Spanish disease" and the first symptom of his encephalitis, the epileptic fits, and, again, an intermission of more than one year's duration before the reappearance of clinical signs, the leftsided hemiparesis. Then, again, about a month later, an oculomotory paresis sets in, rather suddenly.

Case 26. In a woman of 30, who was admitted to my department 9th October 1923 (under the diagnosis of "melancholia"), absence-like epileptiform equivalents occurred at an advanced stage of the disease. In 1918 she had had fever, headache, slight somnolence for some days, no mesencephalic symptoms; she was afterwards in good health until July 1920, when she had a similar but far more pronounced attack, with two months' deep somnolence followed by amnesia. Afterwards, episodically, she suffered from sleepiness, sometimes slight trembling of the hands when she was undressing, or the like, fatigue, loss of hair, disturbances of menstruation. She grew more and more apathetic, and often complained that she "found it so difficult to express her thoughts in words", that she "no longer took any real interest

in things", and that she "could not feel for others as before". During the last few months before her admittance she had developed a gradually increasing motor sluggishness and bradyphasia; she had no power over her legs, "begins by walking fast, but ends by walking slowly". Now and again some myoclonic jerks in left cheek and upper arms. A few days prior to admission she had a fit, of which, in the ensuing period, she has had about sixteen to seventeen in all: suddenly she begins to gaze fixedly before her and to laugh "in a strange manner". This lasts about three minutes, then she seems to come



Fig. 20.

round, though still for about five to six minutes she continues to be absent-minded and "queer". She declares amnesia as to the first phase of the attack. The attacks set in quite suddenly, as though "her senses fled". During the second phase she has a "sensation of being far away", she can hear and understand everything around her, but is unable to utter a sound. Quite suddenly she comes round again, feels tired and generally sleeps for several hours afterwards. There are never any tonic or clonic spasms, nor involuntary micturition, nor biting of the tongue or falling down; at the most there is a slight swaying of the body.

Little by little she grew rather depressed over her condition, but she gave expression to no actual melancholic ideas. She

presented a very typical medium grade of parkinsonism, greasy face, slight myoclonic jerks in the fingers, diminished convergence movements of eyes, marked bradyphasia which, when she became emotionally disturbed, was changed into a rather violent tachyphemia; excessive bradykinesia, bradybasia, suggested, as well as spontaneous, catalepsy (Fig. 20). The humoral syndrome was normal. For a certain period there was rise of temperature up to 38.8° , some tachycardia up to 104; coincident with the rise of temperature she had some hallucinations of hearing, at the beginning invariably nocturnal; she had the idea that she was accused of having syphilis, and on that account fell into moods of despondency; at times her mind was more or less clouded, she had slight delusions of being persecuted by the hospital staff, refused food for fear of being poisoned, etc. While in the ward no true fits of any kind whatever have been observed. Her confused singing was not especially bradyphasic.

Case 27. In a girl, aged 10 years, the chronic encephalitis, also revealed its presence through the occurrence of epileptic equivalents, i. e. absences and somnambulism. The girl was in my department for a week in the beginning of 1924. She had a febrile phase, "Spanish disease", in 1920, with rather pronounced fever, but without more marked cerebral signs. After that, she would not quite recover, was easily fatigued, lost in weight, had dyssomnia. Before her illness, she had been an intelligent, and bright girl, now she would get "absent-minded" and dull for a moment, not reacting to questions, etc. These fits were not accompanied by spasms, but once she passed the urine involuntarily. In the ward, she had a true somnambulism of a few minutes' duration. No impairment of intellect could be detected, nor any neurological signs.

The following Case 28 is of an extremely polymorphous type, and thus summarizes a great number of the symptoms and syndromes previously mentioned. This case is also of the very greatest interest in regard to differential diagnosis; in this respect it may be correlated with Case 61. Before we learned to know the multiform manifestations of chronic epidemic encephalitis, we should, in a case like this, undoubtedly have been content with the diagnosis: brain tumor. Unfortunately, in the present case, I have not been able to confirm my diagnosis of "chronic epidemic encephalitis" by an autopsy. I give below the purely clinical evidence which seems to

me to substantiate the correctness of this diagnosis. Moreover, to make up for the lack of an autopsy, the spinal fluid of the patient, inoculated intracerebrally into rabbits, produced encephalitic brain lesions in these animals (cf. further p. 223).

Case 28. Female, aged 50, married. Admitted 22nd April 1922, died 16th October 1922.

Pronounced maniac-depressive predisposition, herself being of an emotional temperament. In 1922 she had the "Spanish disease" simultaneously with other persons in her home (of whom a son died of the disease). Her own attack was mild, slight fever for about a week, no pronounced lethargy, no cerebral symptoms.

Subsequently she suffered from fatigue, and periodically she was somewhat "emotional". May 1921 she began to get fits, to begin with almost regularly just before noon. She complained of dizziness, she swayed, her speech became indistinct, blurred; she then quickly passed into a lethargic state, with a blank-erratic stare, or with closed eyes, she lay supine with a somewhat snorting type of respiration, jerks in the facial muscles, and mumbling movements of mouth and lips while "froth" appeared round the mouth. (cf. below). Usually she did not answer when spoken to; at other times, again, she would reply by murmuring single words, seeming to understand. There were no involuntary excretions, no biting of the tongue. The duration of the fits was up to some hours. Onset and recovery slow; the fits are said to have been abbreviated by psychic influences (??). She generally declared amnesia as to what had happened during the fits. She had them from two to three times a week, sometimes, however, there were longer intervals; thus, in the summer 1921, an interval of several months occurred; then again exacerbation and, eventually, the fits occurred daily. During the intervals there were no neurological or psychic disturbances, more especially no persistent headache, dizziness, vomiting or visual disturbances.

The day previous to her admission, when I saw her at her home, she had a fit of violent intensity, this time accompanied by left-sided, flaccid hemiplegia, and (transient) Babinski reflex.

The hemiplegia had disappeared when she was admitted to my department.

She was a stoutly-built, well-nourished woman. She was mentally clear; no demonstrable psychic defects. No dystrophic symptoms; no abnormal pigmentation. Diuresis normal. During her whole stay in the hospital the urine was free from albumin,

sugar and urobiline. There was no palpable arteriosclerosis: blood pressure 120 mm. Hæmoglobin (Tallquist) 80 %. No pulmonary or cardiac affections. Liver dulness normal. Thyroid gland normal. The first neurological examination revealed absolutely nothing abnormal: No pareses, no disturbances of muscle tonus, of reflexes or of sensibility; examination of the eyes also showed normal conditions¹); no abnormal involuntary movements. She was perfectly clear-minded, though somewhat depressed on account of her illness; no drowsiness, no headache, dizziness, vomiting, or the like; the temperature was normal; no bradycardia.

The fits of lethargy referred to already occurred during her first week in the ward; now more, and now less pronounced, now of shorter and now of longer duration, but, on the whole essentially uniform in their aspect: a slow relapsing into a state of torpid staring, with divergent squinting, occasionally preceded by a little wailing and screaming and tossing about in the bed; very rapid, fine clonic twitches in various facial muscles, gradually passing into distorted grimacing; smacking, grunting, slightly snorting type of respiration. Salivation, excessive perspiration and congestion; then fairly rapid jerking in right sternocleidomastoid, in both arms and legs, mostly medium rapid or rapid, now weak, now strong myoclonic trembling with but little motor effect (some playing of fingers and toes, etc.). Also a more persistent fine tremor of the right hand. A good deal of myoclonic jerks in the abdominal muscles. Gradually some torsion movements of the entire body: twisting toward the left, slight "arc de cercle", etc. No rigidity apart from some sprawling with the legs; no pareses; no Babinski reflex. Only on one occasion was there any involuntary excretion of faeces; no biting of the tongue; no reaction to ovarian pressure. Rise of temperature never observed during the fits; on a few occasions only, slight bradycardia. No vomiting. The fits lasted for from some hours to all through the day, with a gradual coming round; the patient constantly declared that she remembered nothing of the attacks. The frequency of the fits varied during her stay here as they had done prior to her admission; there was a remission in midsummer, which caused her to ask for discharge. She went home, but was readmitted a fortnight later, and from now onwards there was pronounced progression of the disease. Her fits became more and more frequent and protracted; in addition a different type of fit occurred, in which (1) the hyperkinetic symptoms were confined to the right side of the body while there was a left-sided flaccid hemiparesis with

¹) Except for excessive myopia with peripapillary atrophies.

Babinski reflex; and (2) epileptiform seizures (5 in all) occurred, lasting from a few seconds to some minutes, initiated by screaming, cyanosis, purely clonic spasms, now more markedly in the right, now in the left half of the body; conjugated deviation to the left, sanguinolent froth about the mouth, biting of the tongue, passing of urine; on a few occasions these attacks were followed by flaccid left-sided hemiplegia. (3) Or, again, fits of coarse choreatic jactitation of the head, of right arm and leg, torsions of the body, sighing and semi-hiccoughing respiration, grimacing, now with, now without, clouding of consciousness, lasting for from a quarter of an hour to half an hour.

About the middle of July the left-sided hemi-paresis became more and more persistent, with growing spasticity and flexion contractures, especially of the hand; the Babinski reflex (and knee and ankle clonus) being however extremely inconstant. In the right limbs there was never any definite paresis and only during the fits or immediately afterwards was there occasionally some spasticity (mostly in the leg), and sometimes trace of Babinski reflex. While the true myoclonic jerks gradually disappeared, the right-sided hemi-chorea would now persist, also in the intervals between the fits, to a more or less pronounced degree.

During the last month of her stay the clouding of consciousness grew almost permanent; there was some confabulation, fatuity and euphoria, and impairment of apperception. The speech grew more blurred and slow; no definite aphasic disturbances. Ophthalmoscopic examination (last time 3d October 1922) still revealed no trace of "choked discs" or optic neuritis; pupillary reactions, fields and acuity of vision, eye movements, all were normal. Repeated spinal puncture showed normal figures for cells and albumins. Negative Wassermann test in serum and spinal fluid. X-raying of the skull gave no evidence of brain tumor. Although frequently tested (also subsequent to the fits) the urine showed constantly normal conditions. The temperature curve was on the whole normal, showing, however, at months' interval, sometimes slight rises (37.8° — 38.1°) of some few days' duration, without it being possible to discover any other somatic affection; or, again, all through the month of August, there was a marked tendency to subnormal temperatures, down to 35.1° in the evening, and a morning temperature of up to 37.2° ; that is to say an inversion of the curve¹). The pulse rate

¹) Some few of the hyperthermic episodes seemed to coincide with injections of cacodyle. Subcutaneous injections of $\frac{1}{2}$ cc. of the patient's own spinal fluid produced however no reaction on the temperature curve.

curve was also fairly uniform throughout, 72—90 per minute, and, as has been said, there was only on a few occasions a slight bradycardia (or arrhythmia) during the attacks.

With increasing somnolence, choreatic unrest, fresh epileptiform convulsions, and terminal elevation of temperature (broncho-pneumonia) the patient died 16th October 1922. Unfortunately, autopsy was not permitted.

As far as this patient is concerned also it cannot be wondered at that, for a time, the "lethargic" fits with their peculiar "forenoon" type, their seemingly being influenced by psychic impressions, and, at the same time, the lack of all other signs of any organic nervous affection, aroused the suspicion of hysteria, especially when the emotional temperament of the patient is remembered as well as the severe psychic traumata of different kinds to which she had been exposed just at the time of the onset of her illness (her son died from the "Spanish disease", her sister committed suicide, her daughter became insane).

The general appearance of the fits, with the spasmodic (myoclonic) component, the disturbance of speech, the dizziness and reeling gait, should however arouse a strong suspicion of an organic cerebral affection. This suspicion became a certainty when, during one of the fits, a hemiplegia occurred, with Babinski reflex.

Syphilis could most certainly be disregarded, the humoral syndrome, too, being negative. Likewise, the general picture of the disease, more especially in its further development, was utterly different from the usual features of a cerebral arteriosclerosis, just as, on the whole, the patient presented no signs whatever of a (presenile) arteriosclerosis.

Immediately on her admission the peculiar "lethargic" fits made me think of chronic epidemic encephalitis. The whole course of the illness may be understood by the assumption of this disease. In fact, we have here, as it were, a résumé of a number of symptoms which are found, partially more isolated, in other of our cases: i. e. the "lethargic" fits; the suddenly appearing and

again rapidly vanishing hemiplegia which, at a later stage of the disease, however, becomes persistent; the myoclonic, choreatic, movements, the torsion spasms, occurring during the fits and gradually also in the intervals, and, finally, the epileptiform seizures. The slight oscillations of the temperature curve likewise correspond with the conditions found in chronic encephalitis.

With regard to the differential diagnosis, a brain tumor might certainly be first thought of, more especially perhaps an infiltrating glioma, for instance in the right hemisphere (the frontal lobe). I feel pretty sure, however, that such a polymorphous, phasic-remittent clinical picture, as seen in this patient, would be rather unusual in cases of cerebral glioma. Apart from the lethargic attacks, the usual general symptoms of cerebral compression (such as headache, vomiting, bradycardia, etc.), were totally or almost totally wanting throughout the course of the disease; more especially, there was never the least trace of optic neuritis or papillary stasis. As there was no autopsy we cannot, of course, completely eliminate the possibility of a brain tumor. However, in my opinion, the general clinical picture finds its most obvious explanation through the assumption of a chronic epidemic encephalitis. The result of the inoculation experiments on rabbits (see below p. 223) may also afford some corroboration in favour of this diagnosis.

Later on, I have seen three more cases, the clinical pictures of which were, too, highly suggestive of a brain tumor. But, judging from the further course of the illness in these patients. I feel pretty sure that we have to deal with cases of chronic, epidemic encephalitis.

Case 29. A girl of 15 years, who was admitted to my department December 29th, 1923.

Previously healthy, she had an "influenza" in the beginning of 1920. For some four weeks she was rather ill, with rise of temperature to 40°, drowsiness; no other cerebral signs. After that time she often was seized with fits of stiffness and slight clonic jerks in the left arm and the left side of the face, without loss of consciousness; but after the attack, the left arm

would usually keep paretic for a couple of hours. During a shorter period there was diplopia. No impairment of sight. In the summer of 1920 an ophthalmoscopic examination revealed a pronounced "optic neuritis" in both eyes; visus 5/6; field of vision normal. Slight paresis of right abducens. Left knee-jerk slightly increased, whereas the abdominal reflexes were a little lessened on the left side. Seeing that the girl had had some swollen glands during her earlier years, a neurologist (Dr. Krabbe) suspected a tuberculoma of the brain, and advised a treatment with Finsen light. Before this treatment was commenced, however, a spontaneous amelioration of the girl's condition set in. She was rather well, until August 1921, when the fits recurred, with more pronounced epileptiform features: The fits started with a cry, she fell round, losing consciousness, passing urine, having clonic spasms for 5 or 10 minutes, then subsiding into a somnolent state, after which she would come round again; she had amnesia for the attack. The ophthalmoscopic examination showed normal eye grounds this time. She was treated with tartrate of borax and luminal. Her condition was changing, with fits almost every morning. She got somewhat depressed. A few days before her admission to the hospital, her attacks became rather frequent, 10—12 times a day.

She was a healthy-looking girl, well nourished; no dyscrin-al signs¹⁾. No psychic disturbances, especially no mental torpor at all.

In the ward, she had, during the first week, numerous fits, up to 120 a day. Almost all the attacks had the same semiological features. Without warnings, she is seized with a tonic spasm in the left arm, the hand becoming slightly pronated and flexed, the head and the eyes being turned to the left. After a few seconds, clonic jerks set in in the arm, left side of the face, more rarely in the left leg. There is no loss of consciousness, no tongue biting, no involuntary micturition. The seizures last for a couple of minutes, at most. A postparoxysmal paresis of the left arm is very pronounced, especially in the days when the fits are very numerous. Frequently, the Babinski sign could be elicited on the left side, and there was a persistent increase of the left knee-jerk and ankle reflex. The speech was never impaired, she could even converse with those around her during her fits, thus, like in the classic Jacksonian epilepsy, "assisting in her seizures".

¹⁾ She had menses for the first time in December 1921.

Her fits proved quite uninfluenced by all treatment except large doses of hydrate of amylen. From January 11th 1921, they became less frequent and violent and, gradually, only slight myocloniform, not synchronous, jerks in the fingers, the elbow, the shoulder, left side of neck and face, remained, coming on quite irregularly, persisting for half a day or so, ceasing during the night. The paresis of the left arm had disappeared. She was treated with argotropine. From January 26th till her discharge, February 11th, 1924, she was quite free from fits of any kind.

The neurological examination, carried out during a quiescent period, showed no persistent neurological signs. Movements of eyes, eye grounds, acuity of sight, fields of vision, pupillary reactions, all normal. No pareses of face or limbs, no change in muscular tonus, no sensory troubles, the joint-sense and stereognosis of left hand, too, being unimpaired. After the period of fits the plantar reflexes were of the flexor type. Only when the fits occurred in rapid succession, the patient would complain of headache; there was never vomiting. No giddiness; gait normal.

X-raying of the skull gave no evidence of an intracranial neoplasm. The spinal fluid showed $\frac{1}{3}$ cells, 0 globulins, 8 albumins; the Wassermann test negative in blood and spinal fluid; as was, also, the Sigma reaction.

The temperature only once rose to 38° in the evening and, after the treatment with argotropine, there was once more a rise to $38,3^{\circ}$; otherwise, the temperature was normal during her whole stay in the hospital. The rate of the pulse would now and again get a little high, up to 106 beats a minute. In the heart, a slight systolic murmur could sometimes be heard.

When leaving the hospital, she felt perfectly well.

In the other patient, too, there was an optic neuritis.

Case 30. Married woman, aged 46, who was in the hospital from October 2nd to November 27th 1923.

No history of previous illness, until 1918, when she was laid up for some 10 days with fever and headache, but no other cerebral symptoms. She declares that she has felt perfectly well till May 1923. Her katamenias ceased a year ago.

Since May, she has suffered from rather severe headaches, occasionally with vomiting, giddiness, slight impairment of sight, diurnal somnolence and nocturnal dyssomnia; she has lost in weight and has had some loss of hair. No polyuria or polydipsia. In the limbs and in the trunk she has noticed slight, isolated jerks of the myoclonic type. A few days before her admittance

to my department, an ophthalmoscopic examination showed a marked papillary stasis in both eyes, the swelling amounting to 2 and 3 diopters, respectively.

In the ward, there was no mental torpor at all, no bradyphrenia, nor any other sign of parkinsonism. Slight paresis of lower part of the right facial nerve. No impairment of eye movements; pupillary reactions, fields of vision, normal; swelling of discs as before. No troubles of speech or swallowing; no paresis of limbs; gait slightly staggering. Deep and skin reflexes normal. No sensory troubles, deep or superficial. Stereognosis of hands unimpaired. Examination of acoustic and vestibular functions gave normal findings.

Fine, quick, irregular, vibrating tremor of fingers of both hands, disappearing on complete rest of the limbs, increasing at elevation and, partially, on action. In the feet, too, some tremor was sometimes seen, at rest and, more pronounced, at elevation and on action. No true myoclonia anywhere.

She was a little poorly nourished; weight kgs. 53, hemoglobin 100 % (Sahli). On a few occasions, a slight glycosuria was found (1 % Lohmstein). No pathological findings in heart or lungs. Temperature normal except for a single evening rise to 38°. Rate of pulse not exceeding 88. Diuresis within the normal limits. Blood pressure 150 mm (systolic). Hair of the head rather thin, axillary hair and pubes normal. X-raying of skull showed no reliable signs of brain tumor or enlargement of the sella turcica. In the spinal fluid was found: 0/3 cells, 0 globulins, 9—10 albumins, the Wassermann reaction being negative in blood and spinal fluid. The pressure in the spinal fluid was 200 mm.

During her stay in the hospital, her general condition improved very considerably, so that she, herself, felt perfectly well at her discharge, November 27th, 1923. The swelling of the discs had however increased a little, amounting now to about 4 diopters, without, however, any greater impairment of sight (5/6, 5/12 resp.) or of fields of vision. On the whole, the affection of the optic nerve was stated, by our ophthalmologist, to be that of a true papillary stasis, not that of an optic neuritis.

I should not think that the persisting and even increasing papillary stasis would suffice to make this case one of brain tumor. The disappearance of the other neurological signs would then be rather striking. And, again, the whole clinical picture, even though in some of its symptoms reminding very much of an intracranial growth, does not show any particular features that we have not already met with in our cases of chronic

epidemic encephalitis. The patient has kept all right since her dismissal, and has presented herself several times at the hospital; however, beside the eye affection, there have not been found any objective signs.

Case 31. At present I have in my department a man of 24 years of age who, in 1921, in Holland, was taken rather suddenly ill with fever and somnolence for about a week; there is no reliable information as to ocular signs or involuntary movements. During the ensuing years he frequently suffered from headaches, particularly on the left side, without vomiting. About New-Year 1923 he had some fainting fits and, shortly afterwards, a generalised clonic convulsive seizure with loss of consciousness, these attacks becoming rather frequent as time went on,



Fig. 21.

also during sleep. Subsequent to the first seizure he suffered for some time from diplopia and dimness of vision. Examination of the eyes showed paresis of right n. abducens and right n. trochlearis; the pupils were normal, as were also the visual acuity, visual fields, and the eye grounds. Acoustic-vestibular functions were intact. Right corneal reflex slightly diminished. There was trigeminal anesthesia over an area of about the size of a florin on the right side of the nose, anesthesia also of left half of tongue in the trigeminal region. Doubtful right-sided facial paresis.

X-ray examination of the cranium revealed nothing abnormal. There was no parkinsonism, no abnormal motor unrest, no cerebellar symptoms. Slight rotatory nystagmus when looking towards the right. Speech occasionally somewhat jerky.

During his stay in the hospital the trochlearis paresis disappeared completely, and the abducens paresis abated considerably. Now and again there was a divergent squinting of the right eye. Pronounced impairment of convergence movements was found. Eye grounds remained normal, also pupillary reactions. The corneal reflexes had now become symmetrical. There was continuously a small hypalgetic-hypesthetic "plaque" on the right

side of the nose and the same sensory disturbances in the left side of the tongue (Fig. 21). The facial paresis became doubtful; there was no difficulty of chewing or swallowing; no paresis of the limbs, no rigidity, nor any well-marked hyperreflexia; the plantar reflexe on the right side however being occasionally somewhat dubious. The gait slightly staggering. The temperature curve proved to be rather of the "flat" type; there was never at any time any sign of hyperthermia. All the time, however, bradycardia was present, down to 52 beats per minute. The customary general cerebral signs of brain tumor have been absent; the sensorium is constantly intact. In the ward he has only had one seizure of a few minutes' duration, generalised clonic convulsions, loss of consciousness, no biting of the tongue, no involuntary micturition or postclamptic palsies. Spinal fluid: cells 1/, globulins 0, albumins 5. Wassermann tests in serum and spinal fluid negative. No pathological findings in the urine.

He was given injections of argotropine, and his condition improved very much, the headache, diplopia, giddiness totally disappearing and the gait becoming quite steady. Only a slight squint in the right eye and an impairment of convergence movement of the eyes persisted on his discharge on September 15th, 1923.

Immediately after having left the hospital, his fiancée "gave him up" in a rather rash way. There was no immediate emotional response, he only became a little more "quiet", would sleep more restlessly, with heavy dreams and somniloquia. Sometimes he felt very tired, and he frequently suffered from headache. But he was able to attend to his work, could climb ladders without turning giddy etc.

On December 1st, 1923, he was once more admitted to the hospital. About a fortnight before, he was found one morning in his bed, apparently unconscious, with his body bent backwards in an opisthotonic way, his head being thrust deep into the pillow; alternately, he tossed from one side to the other, the while he smacked his lips, protruded his tongue, etc. Fits like this were subsequently observed during sleep, usually without his awakening, the movements frequently extending over the arms and legs, but without biting of the tongue or involuntary micturition. Sometimes he bruised his elbows, nates, etc. As a rule, the fits did not last for more than a few minutes. He then became more "sleepy", would go to bed at 10 o'clock in the evening, and would not rise until 12 o'clock the next day, and then again he would go to sleep in the afternoon for three or four hours.

In the ward, an attack as described above, of half a minute's duration, was observed, with complete loss of consciousness and generalised jerkings of muscles. During the night he would often toss about in his bed, speak out loudly, etc.

The neurological examination was rather negative, except for a slight paresis of the abductor and the superior obliquus of the right eye. Eye grounds and vision were normal. No disturbances of sensibility on the nose or the tongue were found. The most conspicuous feature was the bradycardia, the pulse rate always ranging between 52 and 61.

After treatment involving 10 injections of argotropine, he was once more discharged.

When Cruchet in April 1917, in collaboration with Moutier and Calmette, described, for the first time in France, the epidemic encephalitis, he designated the disease observed as "encéphalo-myélite subaiguë". And, even though the main site of the pathologic changes produced in the central nervous system by the encephalitis virus, is, doubtless, — as evidenced also by the autopsies made in Denmark —, the brain or the brain stem, an involvement of the spinal cord is of no infrequent occurrence. We have, therefore, clinical pictures which present, sometimes a blending of cerebral, mesencephalic and spinal symptoms, sometimes the latter more or less isolated.

Different writers give very divergent statements as to the frequency of spinal symptoms in epidemic encephalitis, and more especially in its chronic forms. At any rate, these symptoms do not seem to have been observed particularly frequently (Wechsler, Riley¹), Sicard & Paraf, Léry & Gay, Bassoe, Kennedy, Davis & Hyslop, Stern²), Mlle Lévy, and others).

Most usually the spinal symptoms occur, doubtless, as partial symptoms in more complicated neurological pictures, which, on the whole, by their "disseminated" main aspect, their cerebral and spinal cord symptoms,

¹) Arch. of neur. & psych. 1921 vol. 5. 408

²) In 5 out of 106 patients.

present a marked resemblance to other disseminated affections of the spinal cord, such as those due to syphilitic infection, and, first of all, that of disseminated cerebro-spinal sclerosis (*sclérose en plaques*). This symptomatological similarity is not surprising; for, in these affections, the clinical features of the disease will depend primarily on the localisation of the morbid changes within the central nervous system, and not, to any great extent, on their nature or etiology. And, again, as to the mode of onset and the course of development (apoplectiform onset, remissions, "addition" of symptoms, etc.), the chronic epidemic encephalitis presents many points of resemblance to the abovementioned diseases. As will also be observed from my cases, the differential diagnosis may therefore present considerable difficulties.

Case 32¹⁾. Female, aged 17, single, admitted 14th February 1923. Previously of good health, never had any convulsive attacks. Menses from her 13th year, regularly.

"Spanish disease" in 1918 and 1920, was laid up a fortnight each time. In the first attack, at any rate, there was, in addition to slight fever and some drowsiness, some squinting, with diplopia, and slight ptosis. Also some lisping.

Subsequent to the attack in 1920 she has been suffering somewhat from "darts" in arms and legs, some headache, pronounced fatigue, and, periodically, from disturbed sleep.

In May 1922 she had had an attack similar to the present one, but, after a month she was able to resume her work.

In the autumn of 1922 she suffered from pains and a sensation of numbness in right arm and both legs; movements of hands, as well as her gait, became unsteady. No sphincter disturbances. Her difficulties of gait at last compelled her to give up work. She stayed in the "Balders" Hospital from 17th December 1922 to 14th February 1923; she had been admitted under the diagnosis of "hemiparesis hysterica". There was slight right-sided hemiparesis, unsteadiness on the finger-to-nose and heel-to-knee tests in the right side, exaggerated right knee-jerk, doubtful Babinski sign, analgesia over the right leg. The parietic symptoms and the gait disturbances were extremely varying. She complained of fatigue, headache, (no vomiting), giddiness, she became somnolent and dull to an increasing degree; she also complained of pains in the limbs. Some few evenings the temperature rose to 37.9,

¹⁾ Demonstrated in the Neur. Society of Copenhagen 2. May 1923.

the morning temperature however being normal. Occasionally there was some cardiac arrhythmia; otherwise no abnormal findings in the heart or the lungs. No albumin or sugar in the urine.

When removed to my department, she showed no somnolence, nor any other psychic disturbances. Somewhat flabby-pallid-faced. Normal development of secondary sexual characters; abundant growth of hair. No swelling of thyroid gland. Left pupil wider than the right, both reacting well to light and on accommodation; no ptosis nor any other ocular palsies; some nystagmus on glancing sideways. Ophthalmoscopic findings normal; visual fields normal.

No sensory disorders of the face. No paresis of the face or the tongue. The tongue strongly fibrillating, not atrophic. No paresis of the palate; pharyngeal reflex preserved. Speech natural. No myoclonic unrest in the facial muscles.

In the arms, especially the right, there is a coarse, rapid, irregular, arrhythmic tremor at rest, increasing to oscillatory movements at the elevation of the arms. Action tremor during finger-to-nose test on the right, not on the left side.

Now and again darting, medium-rapid, myoclonic jerks in both arms, more pronounced in the right, with small abrupt shryggings of the shoulder, small movements of flexion at the elbow, some playing with the fingers, etc. In the right deltoid marked fascicular fibrillation without motor effect.

Strength of right arm diffusely diminished; normal strength in the left arm. No hypertonia; no muscular atrophies, brisk tendon reflexes.

Now and then slight myoclonic jerks in the abdominal muscles.

In the right leg slight diffuse paresis. The tonus of the legs somewhat reduced, if anything. Brisk knee-jerks without clonus; bilateral ankle clonus, pronounced on the left side. Here, also, (somewhat inconstantly) Babinski reflex; the plantar reflex on the right side is of the flexor type.

Slight tremor in the left leg at rest, and especially coarse static oscillation of the legs when elevated, and action-tremor on the heel-to-knee test. Small, rapid myoclonic jerks in the left leg (sideward twists of the whole leg, playing of the toes, etc.); often, too, protracted persistent tetaniform upward drawing of patella accompanied by fascicular playing in vastus femor.

No asynergia. In Romberg's test tendency to falling towards the right and backwards. Gait with feet wide apart, slightly atactic-spastic. Otologic testing showed normal vestibular functions.

Some pollakuria and dysuria; there was a trace of pus and albumin, but no sugar reaction, in the urine. Diuresis fairly normal. The temperature was $37,9^{\circ}$ on the evening of her admission, later, on some occasions, $37,6^{\circ}$ of an evening; otherwise "flat" curve. Pulse rate varying, with phasic tachycardia (up to 114 a minute), for some days. No conspicuous respiratory disturbances. The patient is a dysregulator. Spinal puncture showed: cells 22, globulins 1, albumins 15. Wassermann test in serum and spinal fluid negative.

During the first part of the patient's stay in the ward there were no disorders of sensibility. About the middle of March she almost suddenly felt numbness of the right leg, without any other marked change in her state, and without rise of



Fig. 22 a.



Fig. 22 b.

temperature, or the like. Objective examination revealed anesthesia, analgesia, and thermo-anesthesia all over the right leg and in the right lower abdominal quadrant, with preserved deep sensibility, and preserved sense of position. There was some diffuse pain in the leg, some tenderness of the nerve trunks, no articular or osseous affection. The previously existing hemiparesis on the right side had become somewhat accentuated; and, now, Babinski reflex was elicitable on the right side, although somewhat inconstantly, whereas it could no longer be elicited on the left side. The myoclonic unrest in arms and legs, the static tremor and action tremor were unaltered. Some days later there was hypesthesia and hypalgesia over the right arm, and over the right quadrant of the thorax. The numbness in the right leg somewhat abated, and the strenght in the right limbs partly returned, in the course of a few weeks. However, a few days later, she complained of pain

and sensation of numbness in both legs; her gait became considerably worse; she walked with feet wide apart, stumbling, swaying; Romberg's sign was now positive. At the beginning of April there were constant disorders of sensation in the right arm and thoracic quadrant. The strength of the right leg was now fairly good, while there was rather marked paresis of the left, and now, again, Babinski reflex on this side with normal plantar reflex on the right. Shortly afterwards she complained of numbness in the right side of the head and forehead. Examination of the sensibility showed hypesthesia and hypalgesia over right half of head and face and right upper thoracic quadrant, while the sensibility of right arm seemed normal. (Fig. 22 a & b). Repeated sensibility testing towards the close of



Fig. 23 a.



Fig. 23 b.

May again showed a most interesting change in the distribution of the sensory disorders (Fig. 23 a & b), viz. a crossed topography, the involvement of the right side of the body now being restricted to the upper trigeminal segment, whereas is found a marked hypalgesia and hypesthesia over the left leg, extending upwards over the left half of the trunc, as far as to the intermamillary line, but with a fine "sparing out" of the sacral segments.

On her discharge, October 16th 1923, the sensory disorders, the pareses, the clonus and the Babinski sign had disappeared; there remained only a slight tremor of the fingers during action or on emotion, and some tendency to morbid anxiety. She had been given 6 argotropine injections.

During the ensuing period she sometimes experienced weakness and numbness in the legs, but, on the whole, she felt pretty well until late in January 1924, when she suddenly

suffered from severe vomiting and headache, no fever was noticed, the temperature being rather low, not exceeding $36,4^{\circ}$ in the evenings. Some few days later she became "paralysed" round the mouth, she could masticate and swallow, but fluids would flow out between her lips. She had considerable difficulty in articulating her words. At the same time the left eye "turned inwards", and diplopia appeared. The right leg would sometimes "catch the ground", causing her on several occasions to fall down. She also felt giddy. Although the facial troubles disappeared in a week, the squinting and the diplopia persisted. There was a considerable loss of the hair of the head and the catamenias became very irregular and scanty.

I examined her once more on February 26, 1924. No paresis of facial muscles or of the tongue were found. Speech was normal. A slight static and action tremor was seen in the arms as also in the legs. In the right *vastus femoris* a continuous vibrating shaking, now and again with slight upward jerking of the patella, was present. Some few rotating jerks in the hip or extension jerks in the right foot were noticed. No pareses anywhere, tendon reflexes moderately brisk, Babinski reflex on the right side.

A marked hypalgesia and hypesthesia were now again found over the left side of the abdomen, otherwise no sensory troubles could be detected. Abdominal reflexes were all absent.

Pupils equal of size, reacting promptly to light and on accommodation. Slight paresis of left abducens with convergent squinting. Acuity of vision $5/6$ in both eyes. Eye grounds and visual fields normal.

A clinical picture such as the above described would no doubt a few years ago have been labelled as "disseminated sclerosis", although perhaps with an additional designation of "atypical form". This diagnosis ought, of course, to be considered in a case like this. Of the classic symptoms of disseminated sclerosis we only find, however, the not particularly pronounced nystagmus. Against this may be named the features which are alien to disseminated sclerosis, namely tremor at rest, static tremor and action tremor and, principally, the myoclonic jerks, which features play a prominent part in the clinical picture. Even though we may occasionally find abnormal involuntary movements in disseminated sclerosis (for instance atetoid movements, such as I have once de-

scribed)¹⁾, neither have I personally seen a muscular unrest of a nature and persistence as in the above case, nor do I remember to have read about it in medical literature.

The lack of any of the classic symptoms of disseminated sclerosis on the one hand, and, on the other hand, the muscular unrest, the nature of the tremor, the slight pleocytosis in the spinal fluid, the onset of the disease after a febrile attack, the somnolent-febrile phase at "Balders Hospital" all these features in connection with our experiences of chronic epidemic encephalitis, leave, in my opinion, little doubt as to the diagnosis.

The disorders of sensibility afford one of the most peculiar features of the clinical picture of the patient concerned. That, notwithstanding their capricious changing of topography, these sensory disturbances are not hysterical, is evidenced both from their topography, as well as by the fact that in their alternation from one half of the body to the other, they follow the doubtless organic paretic attacks accompanied by Babinski reflex, etc.²⁾.

That the disorders of sensibility should be of a purely spinal origin seems highly improbable, in my opinion, especially on account of their topography which constantly, notwithstanding alternation, preserves a hemilateral character, or, again, gives crossed sensory disturbance with segmental involvement of the fifth nerve. The most likely interpretation seems to be a pontobulbar localisation of the encephalitic processes. The partial impairment of sensibility, its alternation and regression, most probably points to perivascularitic lesions. The corresponding movements of the motor symptoms,

¹⁾ Wimmer: Disseminated cerebro-spinal sclerosis. *Bibl. f. Læger* 1910 p. 89 (Case 2).

²⁾ It is perhaps not unnecessary to remark that, besides by myself, the patient was examined by my chief of clinic, Dr. Kn. Krabbe.

more especially the repeated "shifting" of the Babinski reflex from the right to the left side, would likewise be easily explained by assuming a thus localised, essentially perivascularitic process.

Case 33. Male, aged 24, workman, in my department from 28th May to 6th November 1922.

Previously of good health. Towards the end of 1919 he had been confined to bed a few days owing to slight subjective febrilia, but without any pronounced nervous symptoms.

About six months later he had spells of drowsiness in the middle of the day, "would sit in a chair and fall asleep". He slept well at night. From midsummer 1921 he had difficulties of walking, "could not control his legs", and some time later he experienced double vision. Towards the end of 1921 examination of the eyes (performed at the out-patients' department) showed, impairment of eye movements in all directions, most markedly downwards and on convergence. Diplopia corresponding to paresis of both internal recti. Horizontal and vertical nystagmus. Normal pupillary reactions to light and on accommodation. Eye grounds, visual field normal. Gradually, he developed difficulties of speech (bradyphasia). From November 1921 to April 1922 he was treated at "Bispebjerg Hospital" under the diagnosis of "sequels of lethargic encephalitis"; for a long period he was somnolent and apathetic; the temperature was normal, there was bradyphasia, headache, giddiness with a tendency to fall backwards, slight ataxia on heel-to-knee test, bilateral Babinski sign. Spinal puncture gave normal figures for cells and albumins. Wassermann reaction in serum and spinal fluid negative.

While in my department, he often complained of headache; excessive dizziness, positive Romberg's sign. Occasionally vomiting. Normal temperature (except for some days when he had an acute enteritis).

No true somnolence, but he was somewhat apathetic. His immediate memory when tested with Ranschburg's word-pair test, was somewhat impaired; the usual intelligence tests revealed however no distinct defects. He had frequent attacks of spasmodic laughter.

Average state of nutrition. Diuresis not markedly increased; no glycosuria, nor albuminuria (except during the enteritic episode).

Slight drooping of right angle of mouth; no atrophy or fibrillation of the lips. The tongue can be protruded straightly, is slightly fibrillating. Soft palate deviates slightly to the left.

Speech: drawling, slight nasal accent; gradually it becomes somewhat "choppy".

Slight ptosis of both upper eyelids. Slight outward squinting of the right eye; conjugated eye-movements limited in all directions. Diplopia cannot be provoked. Slight trace of horizontal nystagmus. Well-preserved pupillary reactions. Ophthalmoscopic findings, visual field (also to colours), acuity of vision, all normal. Reduced hearing in the left ear (otitis med. chr. supp.); vestibular functions unimpaired. Otherwise, cranial nerves intact; no dysmasia, dysphagia or respiratory disturbances. Rate and tension of pulse normal.

On his admission there were no pronounced pareses in the arms, but fairly marked in the legs, especially in the right. No hypertonia. Brisk tendon reflexes, no clonus. Bilateral Babinski sign. Gait on a somewhat broad base, slightly spastic, sideward swaying.

No disorders of the deep or superficial sensibility. Some unsteadiness in the right leg on the heel-to-knee test. No sphincter disturbances.

Spinal fluid and Wassermann reactions same as in Bispebjerg Hospital.

His condition was, if anything, progressive, more particularly during and after the enteritis in July 1922: aggravation of the speech defects; the eyes grew more and more immobile through increasing involvement of the associated eye-movements; in the right arm there occurred a fairly pronounced paresis, with action-tremor; marked paraparesis with bilateral knee and ankle clonus and very pronounced ataxia on the heel-to-knee test; finally, there was some dysuria. Psychically he had grown rather cretanic.

Notwithstanding a slight remission of the paresis of the legs he was somewhat of an invalid when, on 6th November 1922, he was removed to the Almshouse.

Both the general clinical picture and the individual symptoms in this patient correspond fairly well with what is found in other cases of chronic encephalitis. The "lethargic" attacks, the more persistent state of drowsiness at Bispebjerg Hospital, the bradypphasic, not scanning, speech, the combined pareses of associated eye-movements with dubious nystagmus and without involvement of the optic nerve, the action tremor, all these features tend to confirm the diagnosis of chronic epidemic encephalitis.

Considering the clinical pictures of the last two cases — more especially perhaps that of Case 32 — in the light of our later observations in Case 62, where a diagnosis of disseminated sclerosis was made *intra vitam*, but where the autopsy revealed a chronic encephalitis, I do not hesitate to include here the following case (Case 34). And, the less so, as we have here an acute febrile phase with somnolence and ocular symptoms which, if it had occurred subsequent to 1917 and not so early as 1915, would no doubt have been diagnosed as lethargic encephalitis. Whether the second febrile episode should be regarded as a reinfection or as a febrile relapse is, as already mentioned in p. 97, very difficult to decide.

Case 34. A boy, aged 15, first admitted to the department November–December 1915. The disease had a fairly acute onset, with headaches, vomiting, dedolations in the limbs, squinting, now and again diplopia, drowsiness subfebrile temperature (up to 37.8). There was some rigidity of the neck as well as Kernig's sign, diminished knee jerks, no Babinski sign. Some days after his admission a paresis of the right arm had developed, with abolition of biceps and radial reflexes, and diminished triceps reflex. No muscular atrophy appeared. No abnormal involuntary movements, no ataxia or intentional tremor. The optic discs were strikingly pale and they were sharply outlined. Spinal puncture showed cells $\frac{4}{3}$, globulins 1 (?), albumins 15. Wassermann tests in serum and spinal fluid negative. There was trace of albumin in the urine.

The paresis of the right arm had totally disappeared at the beginning of 1917. Since then he has been well until the end of October 1922, when he had a "cough", high fever (39.5), dedolations in the limbs; no special drowsiness, no cerebral symptoms. This state lasted about four days, after which time he felt quite well again, and got up. A few days later, however, he noticed that he "could not see with his left eye objects to the left of him". Some days before his readmission to the department, 20th November 1922, he had a "tingling" sensation in the legs, with increasing weakness so that, at last, he was unable to keep standing; now and again the legs "slowly approached one another, so that the knees collided". Simultaneously, there was retention of fæces, difficulty of micturition, only small portions of urine being voided, and, on a few occasions, incontinence.

The patient was well-nourished, of healthy appearance, nothing dystrophic was observed. Sensorium intact. Right pupil slightly larger than the left, both showing diminished reaction to light and on accommodation. No ptosis, squinting, diplopia, or nystagmus. Ophthalmoscopy revealed complete atrophy of the left optic disc, partial atrophy of the right. Field of vision normal in the right eye, defective (for white and red object) in the left, as seen in the diagram (Fig. 24).

Cranial nerves unaffected. No disturbances of speech whatever. Upper limbs normal as to strength, tonus of muscles, synergy, sensibility, (both deep and superficial); the tendon

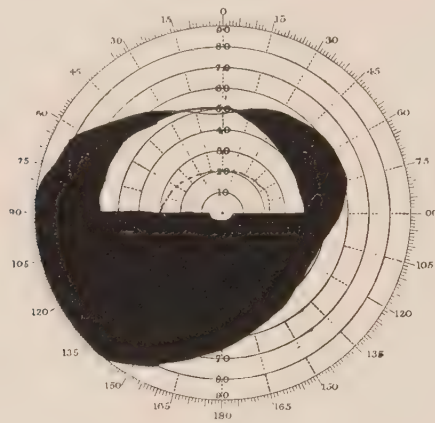


Fig. 24.

reflexes are brisk; Léri's reflex is present on the two sides. There is a very delicate, rapid, irregular tremor in the fingers; no myoclonic twitches.

During the first days of his stay there was a slight paresis of the abdominal muscles and absence of abdominal reflexes.

Flaccid, moderate paresis of both legs; left knee-jerk and both Achilles jerks are absent, also when the patient lies on one side. On one occasion the Babinski sign was definitely elicited in the left foot; otherwise the plantar reflexes were of uncertain type.

There was some fascicular muscular undulation in both thighs. On the heel-to-knee test the right leg behaved in a somewhat paretic-flaccid manner, but there was no true ataxy or action tremor. There was marked thermo-hypesthesia over the legs and the abdomen up to the umbilicus, and hypalgesia and

hypesthesia in the legs up to the groins, more pronounced however on the right side. Sense of movement and position was equally impaired in both legs.

Complete retention of urine necessitated daily catheterisation; a cystitis soon developed.

Spinal puncture showed: cells 25/3, globulins 0—1, albumins 11. Wassermann reaction in blood and spinal fluid negative.

Now and again the temperature rose slightly (the cystitis?). The pulse was normal throughout.

The condition improved in so far as micturition again became normal, the paresis of the legs and the sensory troubles disappeared. A right-sided patellar clonus and bilateral ankle-clonus appeared, however, and also right-sided Babinski sign with a trace of spasticity in the otherwise normal gait.

In this case, again, the "classic" symptoms of disseminated sclerosis are absent notwithstanding the fact that the disease has existed for seven years; its development through phases of fever, its tremor at rest, its initial, flaccid paraparesis with areflexia and sensory troubles, and, in addition, the pleocytosis in the spinal fluid — all these symptoms are much more indicative of a chronic epidemic encephalitis.

We are well aware of the fact that a disseminated sclerosis may have an acute (or subacute) onset; personally, I have, together with Dr. H. Rønne described such a case (with the post-mortem findings)¹⁾. This patient, however, did not present any initial phase of such a markedly febrile-cerebral character as was found in our Case 19; nor do I remember to have found any such mentioned in the literature of disseminated sclerosis. The clinical picture of the latter disease, however, being just as polymorphous, while its etiology is in all probability to be found in a chronic infection, a spirochetosis (Steinert), errors of diagnosis can scarcely be avoided (compare later the chapter on diagnosis).

¹⁾ Rønne & Wimmer: Acute disseminated Sclerosis. Deutsche Zeitschrift f. Nervenhk. Bd. XLVI.

Clinical types of the character of a (more isolated) transversal myelitis and which are believed to have their origin in an encephalitis infection, have been described by Léri & Gay (monosymptomatic spastic paraplegia), by Bouttier, Alajouanine & Gerot (flexion paraplegia coincident with parkinsonism and with associated ocular palsies)¹).

In cases of transversal myelitis, both those with an acute or subacute onset, and those of a more chronic course of development, it is often difficult to ascertain etiological factors, more especially when syphilis, traumatism, gliosis, and the like, are out of the question. In the future we must undoubtedly bear in mind the possibility of a chronic epidemic encephalitis in such cases, just as some investigators (Tobler, Stachelin, Stern, and others) have suggested that certain cases of Landry's ascending spinal paralysis might be due to the encephalitis virus.

Case 35. Male, aged 15, under observation in my department from the 8th April to 2nd September 1922. Previously healthy. Denies syphilis; never takes alcohol; no traumatism of the back.

From June to September 1920 he was treated at the Municipal Hospital, medical department: A week before admission he was suddenly taken ill, with fever up to 39.2° for some days; dedolations in the limbs, though no swelling of joints; and no marked somnolence or cerebral signs.

Later he was healthy until the spring of 1922; when he began to experience a numbness in his legs which sometimes failed him when walking; moreover, he had some difficulty in micturition.

Admitted to my department 8th April 1922; he was pale; worn-out appearance. No palpable arteriosclerosis. Blood pressure 145 mm. Hæmoglobin (Tallquist) 70—80 %. No cranial nerve palsies. No ocular palsies. The pupils react normally; eye grounds normal.

Strength and sensibility of the arms intact; no atrophies; brisk tendon reflexes.

He cannot raise himself to sitting posture without the aid of the arms; no definite pareses of abdominal muscles. Abdominal reflexes lively, cremasteric absent.

¹) Revue neur. 1922, p. 1514.

An almost complete, though not particularly spastic paralysis of both legs, with hyperreflexia, inconstant patellar and ankle clonus, bilateral Babinski reflex. From the toes upwards to the groins there is marked decrease of sensibility to touch and pain, amounting in the feet to total anesthesia. Sense of joint movements decidedly diminished.

Gradually a persistent incontinence of urine (with cystitis) developed.

Spinal puncture showed: cells 25/3 (lymphocytes), globulins 1, albumins 24 (at a later puncture the figures were 22/3, 0 and 12, respectively). Wassermann reaction in spinal fluid and serum negative (in this case also after treatment with mirion for possible re-activation).

On the 2nd September he was removed to the Municipal Almshouses.

None of the usual causes of a myelitis are present here. The findings in the spinal fluid indicate a meningeal inflammatory reaction, and, according to our experiences, the absence of a positive Wassermann test in the blood and the spinal fluid affords an almost conclusive proof against the assumption of a syphilitic myelitis. Our etiological data are thus in reality reduced to the febrile (infectious) attack in 1920. That this attack did not present the "classic" clinical picture of a lethargic encephalitis we know now to be without importance. Other infectious germs than those of epidemic encephalitis might also of course be considered; however, bearing in mind the undoubted prevalence of the encephalitis virus, which we have been confronted with in recent years, and which has by no means disappeared, the most likely suggestion is, in my opinion, that of epidemic encephalitis.

Even though the encephalitic virus does not show a pronounced predilection for the anterior horns of the spinal cord, such as is the case with the virus of the poliomyelitis, it may occasionally settle also in these, as has been evidenced by autopsies (Case 60, Fig. 59) and as may be concluded from clinical symptoms, viz. muscular atrophies. In Case 9, for instance, we had an

isolated atrophy of the tongue, partly unilateral, which was no doubt an indication of a lesion of the bulbar nuclei. Chronic encephalitic amyotrophies of the limbs have also been described, sometimes interpreted as "radicular-neuritic" signs (Sicard & Paraf), sometimes designated as an "atrophie musculaire progressive myélopathique" (Froment & Gennerois), or as an "atrophie type Landouzy-Dejerine" (Gutman & Kudelski).

We need learn more of the post-mortem findings in these cases of a "spinal-amyotrophic type", before we may be able to ascertain the site of the causative pathological lesions. The possibility of a neuritic or radicular-neuritic origin (Sicard & Paraf) might be considered in the cases of more circumscribed muscular affections, such as isolated involvement of the shoulder muscles ("serratus paralysis", Nonne, Speidel, Stern, and others), degenerative muscular atrophy of a hand (Stern), etc. But, even in such cases, and still more when we have, for instance, a bilateral paralysis of peroneal muscles (Hall), a metamerie paralysis of the muscles of the forearm (unilateral), a spinal localisation of the morbid process will suggest itself as being more likely, more especially so if reliable neuritic or radicular symptoms are absent.

Kennedy, Davis & Hyslop believe they have observed a conus syndrome.

In the following Case, 36, there might be plausible evidence of a spinal (bulbo-spinal) origin of the amyotrophies, all the more so as there are other signs of involvement of spinal (pyramidal) tracts. The hypertonia, which is such a predominating feature in the clinical picture, should no doubt be attributed to a degeneration of the pyramidal tracts, even though a strio-pallidal component is made most probable and is also evidenced by some clinical features, i. e. the various forms of involuntary movements.

In this case the clinical picture is in many points strikingly similar to that of an amyotrophic lateral sclerosis

Case 36. The patient is a workman, 36 years old. No predisposition to nervous or muscular affections. He had an attack of pneumonia in 1914, without nervous complications. He denies syphilis.

In his youth, and especially marked then, he often had "jerks" in the body, shrugging of the shoulders, tossing of the head, twitches in the right arm, for instance, with flexion at the elbow while doing manual work; also some kicking with the left leg; no definite jerks in the right leg or left arm, and no tremor while performing every-day movements (such as dressing, eating, and the like).



Fig. 25.

In May 1919 he had "influenza" for about three weeks; he was in bed three days only with a temperature up to 40.1°C. , the rest of the time he was up and about, though feeling slightly feverish; no true somnolence, no mesencephalic signs.

In the early winter of 1919 he had a feeling as if his greatcoat weighed more heavily upon the left shoulder than upon the right; towards December he noticed wasting of the muscles and a weakening in the left hand. At Christmas time 1919 his left leg began to "drop behind" when walking, and shortly after Christmas he discovered muscular wasting and weakness in the right hand also. Almost at the same time he perceived slight difficulty of speech. From that time onwards his state became gradually progressive: increasing rigidity, lack of muscular strength, muscular wasting in arms and legs, increasing difficulty of speech, now and then dysphagia (when he drinks

water "it goes down the wrong way"), and, he developed a tendency to spasmodic attacks of crying. No loss of control of the bladder or rectum.

The patient was admitted to my department April 27th, 1921: he was a well-built, strong man. In bed, he lay as stiff as a poker; he can move his head slowly in all directions, the cervical muscles being however distinctly hypertonic; he can hardly turn about in his bed, and is only able to bend forward to a slight degree but not to raise himself to an erect position, nor to stand or to walk.



Fig. 26.

His face is immobile, mask-like, with too sharply-cut nasolabial lines, the mouth becoming too "square"; there is however no true facial paresis. No labial atrophy or fibrillation. The tongue is freely moved, strongly fibrillating, not atrophic. Movement of the palate intact. Some bradymasia, no dysphagia.

The speech is somewhat bradyphasic, monotonous, slightly nasal tone, not distinctly scanning. Eye movements free, no nystagmus. Pupillary reactions and eye grounds normal.

The arms extremely rigid in extension, sticking to the body, wrists half-flexed, position of the left hand almost "à la griffe cubitale", of the right, "à la main de prédicateur". The legs are in excessive extension rigidity with bilateral pes equinus

(Figs. 25, 26). Spontaneous movements of arms and legs are possible only to a slight extent, slowly, feebly. The tendon reflexes extremely exaggerated in both arms and legs, bilateral ankle-clonus (patellar clonus is not elicitable on account of the hypertonia); there is bilateral Babinski sign.

Marked wasting of the small hand-muscles on the two sides, also slight wasting of the muscles of the forearms (all more pronounced on the left side), no appreciable wasting of the muscles of the shoulder or the upper arm. The legs are emaciated, no elective wasting, however, except perhaps a little in the peroneal group.

Fibrillation and myocloniform jerking in the muscles of arms and legs, and also in the pectorales and deltoids. Spontaneously, or by uncovering, by calling attention to it, or by volitional action of an arm or a leg, the muscular unrest becomes considerably intensified to the point of a coarse shaking of the entire limb, sometimes in the form of extensive choreiform darts, sometimes a not infrequent generalised shaking of the whole body amounting to a violent shuddering.

There is a delicate, rapid, almost uniform tremor at rest in both hands, mostly in the form of pro-supination movements, and more marked on the left side; whenever he lifts the hands slightly, there occur coarse irregular oscillating movements of the whole arm. Intentional movements, however, produce no tremor, neither in the arms nor in the legs.

Electric testing shows complete degeneration reaction in the small hand muscles; partially the reaction is totally abolished, and there is also degeneration-reaction in extensor longus hallucis. In the peroneus and the muscles of the forearms there is a partial degeneration reaction.

Sensibility, sphincter functions, intact.

The patient's temperature remained normal throughout his stay in the hospital. No symptoms from the respiratory organs. Liver and spleen dulness were normal; the urine was free from albumin, sugar and urobilin.

Spinal puncture: cells 2/3, globulins 0, albumins 10; Wassermann test in spinal fluid and serum negative.

During his stay in the ward his state grew steadily worse, to the point of complete helplessness. Gradually some bradyphrenia set in, but no true dementia. September 10th, 1921, he was removed to the Municipal Almshouse.

Intracerebral inoculation on rabbits of his spinal fluid produced encephalitis in these (cf. p. 223).

In the following patient we have a fairly pronounced "Aran-Duchenne" type of muscular wasting.

Case 37. A young clerk, 18 years old, admitted February 24, 1924. He has had several attacks (5 ?) of "Spanish disease" or "influenza", in 1918, 1919, and 1923, lasting one or two weeks. At least three of these febrile attacks were accompanied by pronounced somnolence.

He himself supposes his present illness to be due to an accident about two years ago, when he got both his hands into

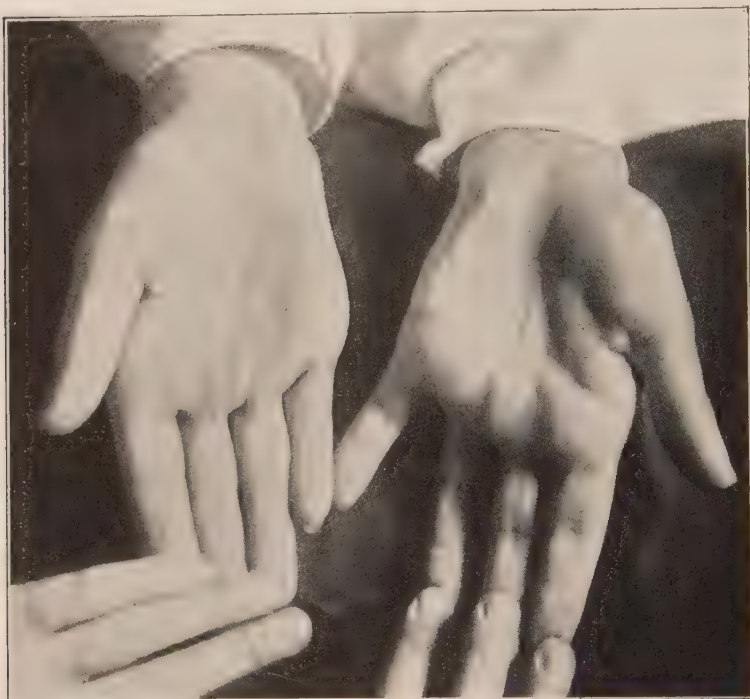


Fig. 27.

the rotating wheel of a bicycle. Some time after that he noticed that he could no longer abduct his left thumb as before. Gradually the spreading of the fingers of both hands and the individual action of the fingers, became much impaired, causing him great trouble when playing the piano. Also the strength of the hands decreased, especially of the left one. Rather violent pains in the elbows have appeared, being however only present at rest. Some few months ago he noticed a wasting of the small muscles of the hands, especially on the left side. There have been no troubles of the legs, no disturbances of gait, or sphincter functions.

For about a year he has noticed myoclonic jerks in the muscles of the arms and the hands. Now and again he has felt a little giddy. No diplopia nor impairment of vision, no disturbances of speech or swallowing.

He is healthy-looking, rather well nourished. No impairment of facial muscles or of tongue; speech quite normal. Reaction of pupils to light and on accommodation preserved, movements of eyes, eye grounds, acuity and fields of vision, all normal.

On both sides there is a marked atrophy of the small muscles of the hands, more pronounced of the interossei of the left hand, with a corresponding impairment of the muscular functions. A "main de griffe" attitude is slightly indicated (Fig. 27). There is no conspicuous wasting of the other muscles of the arms or of the shoulders, and the muscles of the neck are wholly intact. The muscle tone is rather somewhat lessened in the arms. The power of the muscles of the hands and the forearms is moderately diminished, so is also the strength in the tricipites, whereas there is no paresis of the other muscles of the upper limbs. The tendon reflexes of the arms are all present and brisk.

Electrical examination of the muscles shows abolished galvanic and faradic excitability of the opponens and the abductor of the left thumb, while in the right hand the galvanic excitability is still preserved in these muscles. In the other small muscles of the hands is found a partial degeneration reaction, most marked on the left side. The electric formula of the other muscles of the upper limbs is normal.

Occasional myoclonic jerks, not synchronous, are seen in different muscles of the upper limbs. The wasted muscles of the hands may sometimes present a slight fibrillation. In the resting hands, and still more when the arms are raised, moderately fine, rapid tremor occur. There is no ataxia, no dysmetria or adiokokinesia.

The lower limbs are perfectly normal as regards muscle tone, strength coordination, synergy. Tendon reflexes moderately brisk, plantar reflex normal on the right side, whereas, on the left side, an isolated, rather quick dorsal movement of the big toe will sometimes occur. Gait perfectly normal. No sensory disturbances anywhere.

X-raying of the cervical spine does not reveal anything abnormal. In the spinal fluid are found cells 3/3, globulins 0, albumins 12. The Bordet-Wassermann reaction in the blood and spinal fluid is negative. No pathological findings in the urine. "Flat" temperature curve, but no febrile rises. Pulse rate rather low, down to 60.

Three cases more of amyotrophic pareses, due most certainly to epidemic encephalitis, are for the present time in my department. The one, a man of 36, who had an initial febrile stage in 1922, became a febrile, somnolent relapse in October 1923, with a slight remission; but he is still somnolent, bradyphrenic and rather confused, with hallucinations of hearing. He has a paresis and wasting of the small muscles of the hands and, besides, the muscles of the shoulders are atrophied rather considerably. The tendon reflexes of the arms are not increased, the muscle tonus rather diminished. Slight myoclonic jerks and some tremor at rest and on action in the arms. No definite pareses of the legs, no hyperreflexia, no Babinski reflex. The spinal fluid contained 9/3 cells, 0 globulins, 20 albumins, the Wassermann reactions being negative.

The other two patients are girls of 12 and 11 years, respectively. The one has had febrile episodes of some few days duration in 1918 (twice) and in 1923. A few days before her admittance to my department a paresis of the right arm and leg set in, slowly increasing and being rather strong when seen here. There was a marked atrophy of the small muscles of the paretic hand, some hypertonia, increased deep reflexes and, during the first days of her stay in the ward, a bilateral Babinski sign. No myoclonias, but static and action tremor of the right arm. In the spinal fluid was found 11/3 cells (small lymphocytes), 0 globulins, 7 albumins, the Wassermann reactions being negative. The temperature did not rise above 37.6 C. She has had an argotropine treatment, and the hemiplegia has subsided to a surprising extent.

The other little girl is supposed to have had the "spanish disease" some years ago (her brother was ill at the same time). Then she has been well up till 5 weeks before her admittance, when pains, swelling and redness of the left wrist occurred, without, however, rise of temperature. She became somnolent, suffered from headaches, dizziness, and for a short period there was

diplopia. Gradually, pains in the left knee appeared. The neurological examination showed a moderate, leftsided paresis of arm and leg, the facial muscles and the eyes being unimpaired (like in the other girl). There was a rather pronounced, generalised muscular wasting in the left extremities, most conspicuous in the hand, and here a degeneration reaction was present. The deep reflexes were slightly increased, no Babinski reflex; rather a slight hypotonia. Strong fibrillation in several muscles, slight myoclonic jerks, very pronounced action tremor. There remained still some tenderness of the wrist and the knee on passive movements, but no swelling. On the outer side of the left crus the sensibility to touch, pricks and, more especially, to cold was slightly diminished. In the right arm and leg nothing abnormal at all. In the spinal fluid was found 3/3 cells, 0 globulins, 12 albumins, the Wassermann reactions being negative in the blood and the spinal fluid, also when tested with the english technic. Temperature, rate of pulse, normal. This girl, too, has improved very considerably on an argotropine treatment.

Clinical pictures that are predominantly characterised by disorders of sensibility, i. e. neuralgiform chronic encephalitis, are far less frequent among my patients than those of other types. For a fuller description of such cases seen in our department, I may refer the reader to a later paper by my assistant physician, Dr. Kn. Krabbe. Here, I will confine myself to giving a few cases in more detail.

Case 38. At present I am treating a patient who suffers from severe neuralgiform pains in the back of the head, in the left side of the face, in the teeth, and in the left arm; these pains set in during an attack of "influenza" in January 1923. For a time there were slight symptoms of parkinsonism, (slight amimia and bradykinesia), flaccid paresis of the left arm with hyporeflexia, slight tremor at rest, and also static and action

tremor in a mild degree; furthermore there were myoclonic jerks in the right orbicularis oculi, right corrugator, right m. zygomaticus. There was a slight impairment of the tactile and pain sense over the left upper limb and left side of the chest down to the curvature; the deep sensibility being intact (Fig. 28). Spinal puncture showed: cells 40/3, globulins 0, albumins 12. Wassermann reaction in serum and spinal fluid negative. On a few occasions only, the temperature rose to $37,9^{\circ}\text{C}$. otherwise it oscillated round about 37°C . with but small intervals. Treatment with argotropine has caused a considerable improvement in this patient's condition.



Fig. 28.



Fig. 29.

In the case given below, the dominating subjective symptom of the chronic encephalitis is a trigeminal neuralgia.

Case 39. Woman, 52 years old, married; admitted March 18th, 1923. Previously she had, on the whole, enjoyed good health. "Influenza" in the autumn of 1918, headache, fever (up to 39°), "slept all the time"; some "darting" pains in right shoulder; no ocular symptoms; she was confined to bed about ten days.

The second day after she got up, paralysis of right arm and leg suddenly occurred, while face, tongue and speech remained intact. Six weeks later she could again begin to stand on her legs, the arm was much slower to recover; she is still unable to lift heavy things. Simultaneous with the hemiplegia, she was attacked by pains in the right side of the face, these having occurred persistently since then. They come on in at-

lacks, spells of darting pains in the nose, around the eye, ear, along the lower jaw; they are now provoked, for instance, when she blows her nose, eats or speaks. The attacks last for from 3 to 4 minutes, and are accompanied by a flow of tears from the right eye and an aqueous secretion from the right nostril. Injections of alcohol into the trunk of the fifth nerve brought about a relief of the pains for some time.

She has not grown especially fat; no loss of hair; some episodes of polyuria and polydipsia lasting for a few days; irregular menstruation during the last few years. Tendency to dyspnea and oedema around the ankles.

She is strongly built, obese, weight 87 kgs; adipose tissue not tender. There is nothing myxoedematous about her; rather abundant growth of hair on the head and on the body. Slight oedema around the ankles. Findings in lungs and heart normal. Blood pressure 130 mm. The urine is free from sugar and albumin.

Tenderness on the branches of right trigeminal nerve. No corneal anesthesia; the action of the masseter strong. As for sensibility, see below.

No pareses in the face, of the tongue or the eyes; no nystagmus; pupils equal, reacting promptly to light and on accommodation; eye grounds normal. Speech intact.

The muscular strength in the right arm is slightly reduced, diffusely; the tonus is normal, there is no tremor or incoordination; arm reflexes lively.

The legs show normal conditions as far as strength, tonus, coordination and reflexes are concerned; no Babinski reflex. No sphincter troubles.

No myoclonic or other muscular unrest. The examination of the sensibility shows a hypalgesia in the right half of the face, with normal sense of touch; hypalgesia and hypesthesia in the right arm and shoulder, and anesthesia of the forearm and hand (Fig. 29); sense of joint movements intact. Stereognosis preserved.

Spinal puncture: cells 12/3, globulins 0, albumins 8, Wassermann reaction in serum and spinal fluid negative.

From a purely semiological point of view the facial pains of this patient would impress the observer as being a regular trigeminal neuralgia. But, if we bear in mind that the affection had its onset synchronously with the homolateral hemiplegia, that the objective disorders of sensibility involve the right arm beside the face, being

moreover more pronounced and complete in the former, we shall be led to seek for a more central starting-point for these facial pains as well as for the objective disorders of sensibility.

The coincidence of the pains with the hemiplegia might suggest a thalamic lesion, with a transient involvement of the internal capsule, that is to say, something like a "thalamic syndrome" (Roussy). Several of the symptoms belonging to this syndrome are however lacking in our patient; there is neither ataxia, nor astereognosis. And, again, if we correlate the symptoms found in this case for instance with Case 22, we cannot disregard the possibility that the symptoms may have a ponto-bulbar origin, the neuralgia, restricted so completely to the trigeminal region, being perhaps more readily understood by this assumption.

I might also suppose a central origin of some very peculiar hemiparesthetic fits in a patient, who is still under my care.

Case 40. Married woman of 44 years, admitted to my department January 1st 1924. Previously healthy, she has during the last four or five years suffered a good deal from attacks of headache.

About two years ago, her son, who was living with her, had a well-marked epidemic encephalitis. She herself was only taken ill for a few days, with slight fever, but without any cerebral symptoms. Then, she felt perfectly well for about half a year, when one day she was seized with a sudden loss of consciousness, lasting for one or two minutes, but repeating itself ten or twelve times during the following half hour. There were no convulsions, no biting of tongue or involuntary micturition. Afterwards, she had similar fits now and then, and sometimes she would fall round, bruising her limbs, etc. By and bye, she grew rather drowsy during the day-time, whereas her night-sleep was bad. There was a pronounced loss of hair of the head, and she lost 12 kgs. of her weight. No polyuria or polydipsia, nor menstrual disturbances.

During October 1922, she developed fits of another kind, i. e. a sensation of tickling and numbness in the left half of the face and the trunk and in the left arm and leg. These hemi-

paresthesias lasted for about one day and a half. There was no loss of consciousness, no spasm or myoclonic jerks, no post-paroxysmal palsies. In November she had a slight fit of a minute's duration; but as time went on, the fits became more and more frequent, up to a maximum of approximately ten or twelve a day. A spinal puncture carried out in the autumn 1922 by Dr. Schroeder, showed cells 5/3, globulins 0, albumins 10 and a negative Wassermann test in blood and spinal fluid.

In the ward, she showed no mental torpor, nor any other psychic troubles. There were no palsies, no disorders whatever of reflexes, no eye symptoms, no parkinsonism, no abnormal involuntary movements of any kind. And — what was the most striking feature of all — no objective sensory troubles were to be found until April, 1924, when a slight impairment of sensibility to pain and touch was revealed in the ulnar half and the three ulnar fingers of the left hand.

Lumbar puncture showed 4/3 cells (small lymphocytes), 0 globulins, 10 albumins, the Wassermann test being negative in blood and spinal fluid, the Sigma reaction, too, being negative. Radiographic examination of the skull showed nothing abnormal, nor did the otologic and vestibular examinations. Temperature normal but for 37.8° a few evenings, pulse rate a little low (60—68).

In the ward she had several hemiparesthetic attacks, the hemi-paresthesias being frequently accompanied by an ugly taste in the left half of the tongue and a bad smell in the left half of the nose. In some of the fits slight twitchings around the left side of the mouth and some few extension jerks in the left hand were noticed. There was never loss of consciousness nor other true epileptic features.

I think that in this case we may pretty safely exclude the presence of a gross brain lesion, such as a tumor, for instance, seeing that the disease has persisted for one year and a half without developing any of the ordinary signs of brain tumor. The clinical picture fits in perfectly well in all respects with the assumption of a chronic epidemic encephalitis. As to the starting point of the hemiparesthetic fits, I should, in this case, be more disposed to admit a thalamic origin (or perhaps, more generally speaking, a lesion of the "carrefour sensitive"), the hemilaterality being so pronounced and the senses of smell and taste being, too, involved.

3. EXTRAPYRAMIDAL HYPERKINESIA.

In several of the Cases recorded in the previous pages various types of abnormal involuntary movements were observed as manifestations of the encephalitic processes. This muscular unrest constitutes the chief symptom in the clinical pictures we are now going to deal with.

In the majority of the chronic cases of epidemic encephalitis these abnormal involuntary movements, the hyperkineses, are in fact a most characteristic feature, although they cannot perhaps be said to be absolutely pathognomic to the disease, and they should therefore be sought for with the utmost care in cases of uncertain diagnosis.

As far as our knowledge goes at present, we suppose the abnormal movements found in encephalitis to be due chiefly to the morbid processes being localised in the centres and connecting tracts of the extrapyramidal motor system, primarily in the striatal ganglia. Hence the designation: extrapyramidal (striatal) hyperkineses.

This clinical picture may result directly from an acute "myoclonic" initial stage, as has been described by Pierre Marie & Mlle Lévy, among others ("syndrome excitomoteur")¹⁾. Or we may, as in parkinsonism, and in the intermediary types, have an abortive or "ambulatory" initial stage. Or, a shorter or longer interval (up to 4 years, Mlle Lévy) may be interpolated. Or, again, the hyperkineses may coincide with, or overshadow, or, finally, supplant, other previously existing nervous symptoms.

On page 77, it has been mentioned that the muscular unrest is sometimes preceded by (localised) pains, occasionally by affections of the joints ("tuméfaction articulaire"). French authors speak therefore of a "syndrome algo-myoclonique".

¹⁾ Rev. neur. 1920 p. 513.

Encephalitic hyperkinesia presents the most polymorphous clinical pictures, both as regards the type of the movements, their distribution, persistence, etc. Besides by Pierre Marie & Mlle Lévy, minute descriptions have been given by the French authors Cruchet, Sicard, Babinski, Marinesco, etc., and by the German authors Holt-husen & Hofman, Speidel, Gerstmann & Schilder, Boe-stroem, Stertz, O. Foerster, F. Stern, and others.

A differentiation on a semiological basis of the various types of extrapyramidal hyperkinesia found in chronic encephalitis presents great difficulties on account of their multiformity, and of the coincidence of different forms of muscular unrest in the same patient, perhaps even within the same part of the body; etc. We are indebted to Pierre Marie & Mlle Lévy for an important attempt at classification, with which, on the whole, that of Stern fits in very well.

Schematically we may distinguish between four types of extrapyramidal hyperkineses:

- a) Tremors.
- b) Myoclonias.
- c) Choreatic (choreiform) movements.
- d) Athetoid-torsion-like movements.

a) For practical reasons the encephalitic tremor has been described in an earlier chapter, p. 38. It was emphasized, then, that tremor at rest was the form which least frequently occurred¹⁾. Far more often the tremor occurs only on voluntary muscular action, as a more or less coarse "action-tremor" or swaying. Or, again, we have a static tremor in the elevated limb, in the raised head, all over the body when the patient stands erect, up to the point of complete astasia, the patient rolling and swaying like a ship in a heavy sea (case 60). The gait, too, may become severely impaired

¹⁾ It is perhaps not unnecessary to point out how extremely difficult it may often be to make these frequently rather rigid and "contractured" patients assume a position of complete relaxation of the limb involved, the head, etc.

by these disturbances (Cases 43, 44, 59, 60). Strumpell's (more generalising) term "amyostasia" seems to me quite appropriate for this type of hyperkinesia.

As regards rhythm, rapidity, uniformity and amplitude, these forms of encephalitic tremor vary considerably from one patient to another, nay, even in the same patient from one day to another. Sometimes, moreover, the tremor will disappear and recur in the most capricious manner.

The localisation of the tremor is also very varying: It may be hemiplegic, monoplegic, facio-lingual, "tremor of the eyeballs" (Case 60), of the lower jaw, shaking of the head, etc., etc. Again, a tremor which is essentially localised may by attacks become generalised (Case 44). At the same time it is frequently observed that a tremor eventually passes into choreiform movements, sometimes even with the addition of a torsion spasm component, as, for instance, in Case 31.

In my opinion it is far from being the case that tremors — more especially the static and action types — belong chiefly to parkinsonism; I believe them to be found still more frequently in other forms of chronic encephalitis, which might indicate that the tremor, and the akinetic-dystonic syndrome, "parkinsonism", are governed by different patho-physiological mechanisms.

b) *Myoclonia*. A very frequent form of extra-pyramidal hyperkinesia in chronic epidemic encephalitis are the myoclonic jerks: brusque, more or less rapid, up to the point of lightning-swift twitches in individual muscles or muscle groups. The comparison between these jerks and the muscular contractions provoked by moderately powerful or weak galvanic currents (Sicard, Mlle Lévy; "galvanoid twitches", Stern) seems in most cases fairly adequate.

The twitches or jerks may occur sometimes as quite isolated jerks, sometimes in short spells of 3 to 4, more frequently, however, at any rate periodically, in more persistent series of a rate varying between 30 to 40 twitches a minute (Case 41), and 120 to 150 twitches

a minute (Cases 46 and 62). In these more chronic myoclonias there is often a certain rhythm (Sicard); this is however far from being the case always, so that there is scarcely much reason for distinguishing these types of myoclonias by a special name, "the myorhythmias" (Cruchet).

The individual jerks are often equal in respect of amplitude; this may however also vary considerably from one patient to another, and from day to day in the same patient. Sometimes the muscular responses are so great that the jerks become in fact not much different from the clonic spasms observed in other cerebral affections. On an average, however, the encephalitic myoclonias are of mean amplitude, sometimes quite small jerks. And, moreover, there seem to be gradual transitions to the merely fascicular muscular fibrillation (myokymia) without motor effect, as is also mentioned by Foerster. The rate and amplitude of the myoclonia may be influenced by psychic factors, by fatigue, cold, etc. Usually it will persist during sleep, or only decrease to a slight degree; it may however also completely cease (Case 46).

The seat of the twitches varies to a great extent; on the whole, it may be said that they keep rather persistently to the region in which they have first settled down. A generalised myoclonia, extending to most of the muscles of the body, is rarely seen in chronic encephalitis. Localised myoclonias are the rule, either within a single part of a muscle (of the deltoid, the vastus femoris, for instance), or in isolated muscles, more frequently however in muscle groups, in certain combinations, not infrequently revealing the character of a synergic grouping. Thus we have "facial ties" (Babinski, and others), "yawn-ing-tics" (Cases 7, 10, 12), combined twitches in the facio-glosso-masseter group¹⁾, in the cervico-deltoid-pectoral

¹⁾ One of my patients (with parkinsonism) showed moderately rapid, "licking" movements of the tongue outside the lips and (synchronously) myoclonic jerks in the right, slightly rigid, half of face.

group, or in the cervico-scapulo-brachial muscles (Case 58), in the leg muscles, or, very frequently, in the abdominal muscles, the intercostal muscles, the muscles of the back (Case 41), the diaphragm (Sicard), "hemiplegic" types (Case 45), etc. The possibilities of variation are many¹⁾. In these combined myoclonias the twitches often occur synchronously in the affected muscles (Case 58).

The myoclonic disturbance may periodically appear as myoclonic paroxysms, as seen in Case 41. Furthermore, this case shows the exacerbation of the myoclonia as a true "myoclonic relapse"²⁾.

Some of the respiratory disturbances mentioned previously may doubtless be interpreted as respiratory myoclonias, chiefly the "paroxysmal hiccough".

c) *Choreatic* (choreiform) muscular unrest. Semio-logically this form seems to me not to differ much from the muscular unrest found in Sydenham's chorea. We have also here intermittent, incoordinated, "aimless", irregular jerking and tossing movements, sometimes larger, sometimes smaller in amplitude, sometimes more, at other times less brusque, usually arrhythmical, sometimes involving a few, sometimes more groups of muscles, on occasions, again, increasing to a kind of muscular delirium ("folie musculaire") which is, however, but rarely seen in chronic encephalitis.

This choreatic unrest may also be more generalised, most frequently however it is localised (hemiplegic, monoplegic, facial, in the form of grimacing (Case 42), etc.). Being extremely varying as regards amplitude and rate of the movements, it is rarely persistent, but shows a tendency to occur in paroxysms. This form also may to a certain extent be influenced by psychic factors, by

¹⁾ An "alternating" myoclonia (right arm, left half of the face), is mentioned by Mlle Lévy.

²⁾ Mlle Lévy states that long after the myoclonia has subsided, an "état myoclonique du muscle" may persist; "on peut alors faire réapparaître celle-ci par l'excitation faradique du muscle, ou par la simple percussion au marteau".

fatigue, etc., and it may sometimes, unlike myoclonia, be volitionally checked or even totally suppressed; during sleep it will frequently disappear (Case 46). Complete resting position of the patient seems however not to have any strikingly soothing effect on this form of motor disturbance.

Sometimes it may be replaced by a more tonic hyperkinesia, the facial grimaces may thus, for instance, develop into a more persistent "masque de crispation"¹⁾, the chewing movements into a trismus (Case 46).

d) Athetoid, torsion-like movements. "Bradykinesia" (Pierre Marie & Mlle Lévy).

From the above-mentioned more massive, more "jerk-ing" motor disturbances there are evidently all grades of transitions to a fourth form of hyperkineses, manifesting themselves as more slowly and uniformly appearing, more complex and ample movements, usually of the character of rather complicated synergic combinations in which an athetoid and more especially a torsion-like component generally enters.

These extremely varying and grotesque types of hyperkinesia are somewhat differently described and termed by the various writers. Pierre Marie & Mlle Lévy describe these movements under the designation "bradykineses", a term which is perhaps a little unfortunately chosen seeing that it had already been accepted as denoting the motor sluggishness found in parkinsonism. Stern seems, in the main, to classify these movements as "tetaniform spasms".

According to Pierre Marie & Mlle Lévy we have to deal with slow, regular, rhythmical movements, of large amplitude, chiefly localised to the root of the limb, usually combined, for instance involving one arm and one leg, and then most usually synchronous. In one of the patients observed by these authors, for instance, there was a slow elevation of the flexed arm to the horizontal

¹⁾ Sicard & Forestier. Arch. neur. 1922. p. 1122.

level with synchronous flexion in the hip and elevation of the tip of the foot; these "strictly rhythmical" movements were repeated about 40 times a minute, giving the patient "l'aspect d'un polichinelle dont on tire les ficelles d'un seul côté" (Mlle Lévy). If the movements have their site in the cervical muscles, the picture may resemble that of a spasmodic torticollis¹⁾; if the muscles of the trunk are affected, we get "saluting movements" such as deep forward bowings, torsions, "snake-like writhings", perhaps with synchronous twistings of the arms, athetoid-dissociated sprawling of the fingers, etc. Similar movements may also occur during walking; in one of Mlle Lévy's patients, for instance, the movements consisted of an elevation and inward rotation of the arm, "comparables à ceux des grands oiseaux lorsqu'ils ouvrent leurs ailes". The patient's gait will often be compromised by such movements.

It is quite evident, and will be readily understood, that these special forms of motor unrest have caused Pierre Marie & Mlle Lévy some difficulty in regard to classification. Originally described under the designation: encephalitic chorea, these movements are now by these authors parallelised with the athetoid movements, or with those of torsion spasm. According to my observations they do belong to these groups, semiologically; and the same, I would say of Mlle Lévy's "mouvements pseudo-choréiques rythmiques".

The movements here concerned are involuntary and to a certain degree continuous, at any rate not "irregularly intermittent" (F. Stern); they are monotonous, chiefly occurring within one and the same muscular region, slow, usually rhythmical and, finally, they are often combined with, or pass into, more permanent torsion postures. Again, in the distal muscular regions (fingers, toes) we have often simultaneously typically athetoid, slowly

¹⁾ Förster has seen a spasmodic torticollis residual to an originally generalised encephalitic athetosis, and, in another patient, an athetosis developing out of an initial spasmodic torticollis.

creeping, tentacular, dissociated movements (for instance in Case 46). All these features differentiate these movements from the more usual choreatic types; that we may find combinations here, just as well as in the other types of extrapyramidal hyperkineses, is a different matter.

The semiological picture of this type of hyperkinesia will in certain cases be remarkably similar to that of *torsion spasm*. Cases of encephalitic torsion spasm have been described by Bériel, Ramsey Hunt, Grossmann, Pierre Marie & Mlle Lévy¹⁾, Mourgue²⁾, Boestroem, A. Foerster, R. Bing³⁾, Zeiner-Henriksen (Norway), and others⁴⁾. The patient mentioned as Case 46 gradually assumed this aspect to a considerable degree; Case 47 affords a fine example of a "hémispasme de torsion". That this is a question of a symptomatological similarity, only, and not of a nosological entity, seems to be beyond doubt. The progressive (infantile) torsion spasm (Thomalla, Wimmer), the Wilson's disease, and the Westphal-Strümpell's pseudosclerosis form together a well-defined nosological group, "the hepato-lenticular degeneration" (H. C. Hall), having its specific pathologic lesions.

The athetoid and torsion-like movements may, like the other encephalitic hyperkineses, have a varying distribution over the body (unilateral, monoplegic, etc.). The influence of intentional movements, of psychic impressions, etc., upon this muscular unrest also varies: sometimes the hyperkinesia will decrease or even totally disappear, while, in other patients it may very noticeably increase. During sleep the muscular unrest usually subsides (Case 46), not always, however; the true torsion spasms will most usually persist during sleep (Cases 46, 47).

¹⁾ Revue neur. 1922. p. 570.

²⁾ Arch. suisses de neur. & de psych. 1922. vol. 8. p. 163.

³⁾ Archives suisses de neur. & de psych. 1924. vol. XIV. p. 80.

⁴⁾ In a case of parkinsonism in a child reported by Paulian & Grigorescu, there was also, partially, an indication of torsion postures (Revue neur. 1922. p. 1403).

Apart from such cases as, for instance, 41 and 58, most of my cases in which the hyperkinetic component is the predominating feature, show an extremely polymorphous medley of hyperkinetic disturbances, as seen, also, in the cases that have been recorded in other countries. This is however not to be wondered at if we consider the scattering over the various parts of the brain of the encephalitic processes.

Hence, also, the difficulty of undertaking, in individual cases, a sharp semiological differentiation between the various forms of hyperkinesia, such as, for instance, the choreatic and athetoid forms.

Moreover, other peculiar muscular disturbances may sometimes enter as components in the hyperkinetic pictures; for example more persistent tonic contractions of single muscles (or groups of muscles), such as the vastus femoris, with a drawing up of the patella, and a fine rhythmical tremor in same. Or, again, a clonic twitching may stiffen into this type of persistent spasm (Case 7).

Generalised tonic spasms, for instance with a maximum backward bending of the trunk, to the point of the typical "arc de cercle", may occur as phases in other kinds of muscular unrest (Case 46).

There is, on the whole, a tendency to a change in the general muscle tone, in hyperkinesia. The change is, however, but rarely in the form of a persistent hypertonia, it more often shows itself as a *spasmus mobilis*, more especially in the athetotic forms (cf. my cases).

It is hardly surprising, finally, that we may find also other neurological symptoms, such as have been mentioned earlier. Nor is the fact that hyperkineses often run parallel with other "irritative" phenomena (certain psychic disturbances, dyssomia, and the like).

While the hyperkineses may, as has already been pointed out, overshadow or replace previously existing encephalitic nervous syndromes of a different type, the reverse is rarely observed, i. e. that, for instance, an

originally myoclonic picture changes into a parkinsonian one (H. Claude, Meige).

Hyperkinesia may improve or even totally disappear (Case 41); other of our cases, however, show a distinct tendency to persist, leading to a fatal issue, frequently with increasing general cachexia, as mentioned p. 31.

Case 58 affords a fine illustration of a localised hyperkinesia; this case will not, however, be mentioned until later in another connection. A similar, febrile myoclonic relapse is seen in Case 41.

Case 41. A married woman, 44 years old, admitted February 7th, 1923. No serious physical illness previously, twice normal parturition.

"Spanish disease" in 1919, two days' confinement to bed, fever up to 38° , drowsiness, fatigue in the back; no ocular symptoms, nor muscular unrest.

Afterwards: persistent weariness, disinclination to work, no true depression; sleep was fairly good until later on. Headache; somewhat frequently fits of vertigo: "everything going black"; on a few occasions fainting with falls to the ground. Gradually, some stiffness in the limbs, now and again rheumatic-like pains in various parts of the body. No parietic attacks; no visual disturbances.

Sometimes, when using her right arm, she felt a "start" in the same, so that she spilled water out of a glass, or the like; occasionally similar "starts" in the legs when walking, so that "her knees gave way under her".

More characteristic, however, were the pronounced attacks of muscular twitching, lasting from 2 to 3 days, occurring at up to 3 weeks' intervals. These attacks consist in isolated single jerks, occurring at up to one hour's interval, as a sudden, painful contraction of the lumbar muscles (she "can feel it with her hand") and in the abdominal wall with "gasps" (cf. below).

There were no subjective febrile signs with these jerkings; when the temperature was measured, on a few occasions, it never exceeded 37.5° .

She has grown very fat following upon her attack of "Spanish disease", has taken on 25 kgs. in weight; her hair drops off to a great extent; calamenias have become irregular. No polydipsia or polyuria.

She is well-nourished, "pendulous stomach". Weight kgs. 68.900. Appearance neither presenile, nor myxoedematous. Scanty growth of hair on the head, and scanty pubes, only slight trace of axillary hairs. Brownish complexion, no pathologic pigmentation of the skin.

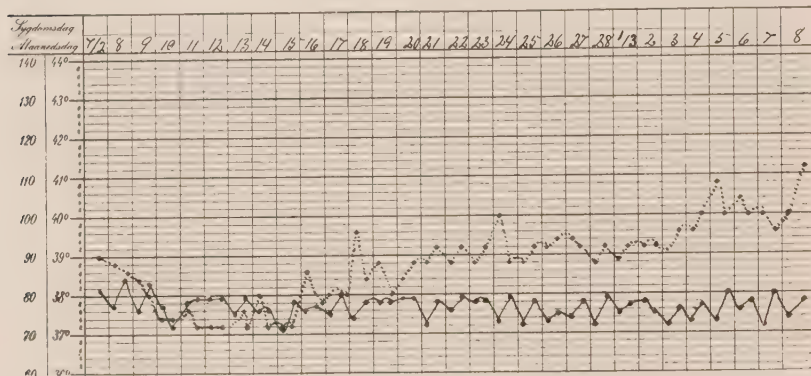


Fig. 30 a.

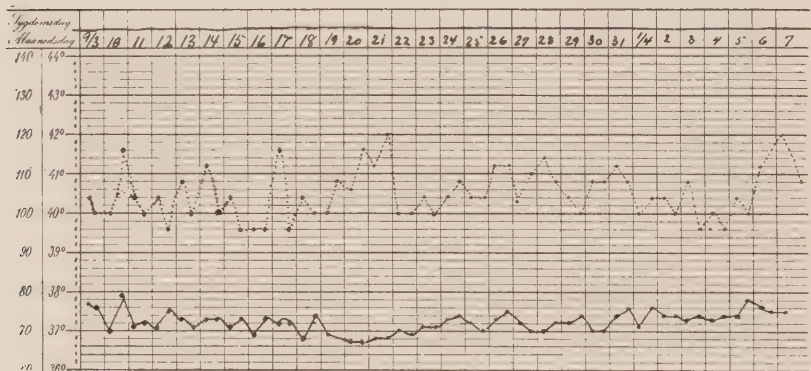


Fig. 30 b.

Psychically she is clear, not bradyphrenic; somewhat worried by her pains and muscular unrest. Mask-like face absent, though skin of the face a little greasy; no facial, glossal or palatal palsies. no persistent disturbances of speech (see later). Eye movements free, no nystagmus; no corneal pigmentation; pupillary reaction to light normal; the reaction on accommodation is somewhat diminished. Eye grounds normal.

Neither palsies nor rigidity in the limbs; moderately brisk tendon reflexes; no clonus; plantar reflexes flexion.

Finger-to-nose test is performed promptly with the right arm; with the left it is compromised by sudden small side-jerks in the shoulder; there is no intention tremor, nor any true action tremor. Slight, moderate, irregular static trembling in the lifted arms. Heel-to-knee test is performed promptly on the two sides.

The entire trunk is shaken by jerks, accompanied by half-smothered gasps or slight hiccoughing. These jerks occur sometimes as isolated instances, sometimes in spells; the inspiration becomes simultaneously "saccadé" and panting, the speech jerky.

The motor effect is provoked especially by myoclonic jerks in the abdominal muscles, now on one side, now on the other, now in the supra-, now in the infra-umbilical segment, with a topping up of the abdominal wall, but without any appreciable displacement of the navel. In the intercostal muscles and the long muscles of the back, jerks also sometimes occur. Finally, there are myoclonic jerks in the muscles of the thighs, slight rotation in the hip joints, extension-flexion jerks in the knees, small twitches in the adductors, while, now and again, light side-jerks in the feet appear. The motor effect is, however, on the whole but slight in the legs, the rotatory movements being the more pronounced. In the right vastus femoris, muscular fibrillation often occurs with up-drawn and fixed patella, but no true motor effect.

The rate of the myoclonic jerks in the abdominal wall is about 30 to 40 a minute. The twitches are not quite uniform, not definitely rhythmic, not synchronous with the jerks in the legs.

In the right deltoid, a few small jerks can be felt by palpation, though not seen; there is no muscular unrest in the other brachial, cervical or pectoral muscles. No athetoid or choreatic movements, no torsions.

Sensibility, sphincter function, intact. There are pains in the calves, which are tender to pressure.

Blood pressure 110 mm. Findings in lungs and heart, negative. Strikingly reduced liver dullness. The urine was free from albumin, sugar and urobilin (repeated tests). The diuresis was usually low. Blood-sugar 0.096—0.092. Test for acid regulation proved the patient to be a dysregulator.

The curves attached (Fig. 30a & b) shows the temperature conditions of this patient; notwithstanding the fall in the temperature a considerable tachycardia persists.

Spinal puncture: cells 15/3, globulins 0, albumins 7—8; Wassermann reaction in cerebro-spinal fluid and blood negative.

A constantly increasing improvement of this patient's condition was seen under treatment with luminal (ctgr. 5) and antipyrin (ctgr. 50)), morning and evening (the luminal was for some time replaced by somnifen gtt. 30, owing to an exanthema); the fever and the pains disappeared, and the myoclonias also gradually subsided; in addition, the patient lost some of her obesity. Spinal puncture, carried out 24th April 1923, showed: cells 3/3, (small lymphocytes), globulins 0, albumins 9. On the 30th April 1923 she was discharged as cured.

This case need hardly be further commented on; some of the features peculiar to it have been previously pointed out.

In the following patient the occurrence of the hyperkineses was much retarded, these symptoms being preceded for a long time by mental troubles of a more general character.

Case 42. Unmarried housemaid of 35 years, who was for the first time admitted to my department on December 12th, 1922. She had the "Spanish disease" in the spring of 1922, her mistress at the same time being ill with, and dying of, the same disease. The patient's attack was a very slight one, of some few days' duration only. But she continued to feel tired and nervous, depressed, with fits of anxiety; she would shun company, slept badly, suffered from headaches, and would sometimes feel rather giddy. No vegetative troubles.

At her admittance, she was somewhat depressed, showed rather immobile features and a marked motor inhibition; the voice was a little drawling; sometimes she was rather somnolent. A most thorough neurological examination showed no neurological signs whatever of a chronic encephalitic condition. The spinal fluid presented 3/3 cells (lymphocytes), 0 globulins, 9 albumins. The Wassermann test negative in blood and spinal fluid.

The temperature was rather subnormal. Slight signs of a tuberculous affection of the lungs being detected, she was, on January 13th, 1922, transferred to a medical department, from where she was discharged after three months' treatment.

At about that time, those around her noticed that she had become slower in her movements, more "dull", did not care properly for her personal cleanness, did not attend to housework as before, grew meagre, ate poorly. Grimaces were now seen in the face, such as pouching of the mouth, curling up of

the nose, etc. She still had frequent headaches, giddiness, dyssomnia. Ultimately, she became a little delirious in the night, with visual hallucinations (of white horses), anxiety, and was once more admitted to my department on January 17th, 1924.

This time, too, she was a little drowsy, but on being awakened she was fully orientated. She was a little slow of thought, and there was a marked bradyphasia, the voice, too, being somewhat hoarse and dysphonic.

There was a slight drooping of the upper eyelids, with overacting frontales; no impairment of movements of the eyes; pupillary reactions, eye grounds, acuity of vision, visual fields, normal. No facial palsy. The mouth and, to a certain extent, the skin of the nose, are very frequently agitated by rather slow, grimacing movements, resulting in protrusion of the lips in a muzzle-like way, a "broad smile", a "crying expression", etc., "turning up" of the nose, and the like. Moreover, in the small muscles of the chin and the right cheek, isolated, quick, myoclonic jerks are seen, though these do not form part of the grimacing movements. These are inhibited by active movements of the facial muscles. The tongue fibrillates violently. There is no atrophy of lips or tongue. No difficulties of swallowing.

In the arms no muscular unrest was seen, whereas, in the toes, some slight extension jerks were sometimes present. No true tremor of the arms or legs. No myoclonias in the abdominal muscles.

Muscular strength of the limbs, muscular tonus, normal. No marked bradykinesia, no Parkinsonian carriage. Tendon reflexes brisk, no clonus, no Babinski sign, no sensory troubles. Spinal fluid showed 2/3 cells, 0 globulins, 10—11 albumins. The Wassermann reaction was negative in the spinal fluid, whereas in the blood, tested with the Harrison method, it was just positive (+ +). A blood test, carried out a month later, after she had been treated with argotropine, but not with any antisyphilitic remedies, showed once more a slightly positive Wassermann reaction. (Her fiancé gave a strongly positive reaction in the blood).

Only on one occasion the evening temperature rose to 37.8°, being otherwise normal, with a rather "flat" curve. The rate of the pulse is usually a little excessive, up to 104. The affection of the lungs seems for the present quite inactive.

Although, in this case, the Wassermann reaction in the blood is positive, I should not hesitate to put it down as a typical case of chronic encephalitis of the hyper-

kinetic type, showing delayed occurrence of neurological signs. Even admitting a previous syphilitic infection, I should contend meself by stating a mere "association morbide", the Wassermann reaction being negative in the spinal fluid, the chronological clinical relation to the encephalitis infection being very conspicuous and, finally, the clinical picture being very unusual to a syphilitic disease. May be, also, that her syphilitic infection is posterior to the encephalitic one.

In the case which follows, the most conspicuous feature is the "amyostatic syndrome", associated, however, with another form of hyperkinesia: myoclonias. In this patient, as well as in the ensuing ones (Case 44, 45) the hyperkinesia is unilateral or remains so for a long time.

Case 43¹⁾. The patient is a shop-assistant, 26 years old, admitted the first time June 18th, 1921. Three years ago he had had gonorrhea; he denies having had syphilis. Neither intestinal trouble, nor jaundice.

In the spring of 1918, and the autumn of 1920, he had attacks of "influenza", i. e. rather high fever, drowsiness, but no other cerebral signs; he remained in bed only a few days each time. Afterwards he was in good health until the beginning of 1919, when his hands began to tremble, especially the right one; his handwriting became bad. For some time he suffered from grimacing of the face ("the mouth drew itself upwards"). Somewhat later he noticed a weakness of the knees, the gait becoming unsteady, reeling. Now and again his speech grew indistinct, as if "the words stuck in his throat". No difficulty of swallowing. He often complained of dimness of vision, no diplopia. No compulsory laughter or weeping. His memory momentarily failed him now and again. His state was gradually progressive.

On his admittance he was a man of average physique, and of a healthy appearance. No palsies of cranial nerves. Pupillary reactions, visual fields, eye movements, eye grounds, all normal; slight nystagmus in extreme side-positions. No corneal pigmentation. Sometimes his speech becomes a trifle "out of breath", jerky. No difficulty of swallowing.

¹⁾ The case has been demonstrated to the Neurological Society of Copenhagen at the October meeting 1921.

No muscular unrest in face or tongue. In the right arm there is both a fine, moderate tremor at rest of hand and fingers, and a coarse oscillatory action tremor, fairly rhythmic in character, in the form of adduction and abduction movements at the shoulder-joint, flexion and extension movements in the elbow, pro- and supination of the hand, spreading and joining and other "sprawling" movements of the fingers. On the finger-to-nose test he cannot keep his finger quietly on the tip of his nose; it is extremely difficult for him to button up his clothes, and the like performances. In his handwriting, too, the muscular unrest is most conspicuous (Fig. 31). In his left arm there is no tremor, neither at rest nor on action; in the elevated legs some

Efter min Fødselse er min
~~min~~ Lydelse opbevaret af den danske Lyd-
samt jeg har haft 2 Søsner. Det har set sig til
en fuld Byrdel i de 4 Aars, og mindre i
i at bruge indtækte, Hænde, hvilket ~~for~~ jeg
gæder mig ~~for~~ nokke jeg en ^{hænde} ~~hænde~~ ~~hænde~~
for min Gang ~~hænde~~ jeg havde ~~hænde~~ ~~hænde~~ ~~hænde~~
første Gang i ~~hænde~~ 1888. og anden Gang
i Efteråret 1897 jeg var meget ~~hænde~~ ~~hænde~~ ~~hænde~~
junge og første Gang var min Hals og
Hænde ~~hænde~~ angrebene

Robertson Dec 28/87

Fig. 31.

coarse trembling. His gait is compromised by excessive shaking and swaying of the whole body, a stamping each time he puts his foot to the ground; he can only walk with support. In a standing position there is a strong oscillation of the head from side to side, and also a pronounced shaking in the right arm when the latter hangs down. Slight myoclonic unrest in abdominal and leg muscles.

No paresis or hypertonia in the limbs. The tendon reflexes are brisk, but no clonus can be evoked. Plantar reflexes are of pure flexor type on the two sides. Sensibility (both cutaneous and deep), and stereognosis in the right hand, intact. Romberg's sign not present. Exercises à la Babinski negative.

Liver dulness normal. No albumin, sugar, urobilin or bile pigments in the urine.

Spinal puncture: cells 9—10/3, globulins 1, albumins 15. Wassermann reaction in serum and spinal fluid negative.

His state became worse, if anything, during his stay in the hospital (up to 17th September 1921); repeated examinations during a second stay in 1922, showed continued progression of the amyostatic symptoms, without however any addition of symptoms from the pyramidal tracts, parkinsonism, or the like; and without impairment of intellect.

Case 44. A young clerk, 18 years old, admitted the first time 10th August 1920¹⁾. He had previously enjoyed good health, except for "rheumatic fever" when he was ten years old. In the autumn of 1918 and in February 1920 he had the "Spanish disease", i. e. fever, headache, but no cerebral troubles. Subsequent to the latter attack he gradually developed a tremor in the right arm, coming on in attacks, and eventually spreading to the shoulder. To begin with these attacks lasted 4 to 5 minutes, though later upwards of 1/2 hour. During the last 2 to 3 months he has had slight speech trouble (it is difficult for him to speak the first word).

He is of healthy appearance, a well-nourished, vigorous boy. No palsies of cranial nerves. Pupils well reacting, eye movements free, no nystagmus, normal eye grounds. Speech somewhat bradyphasic, more especially noticed at the onset, gradually also with a slight nasal tone; no scanning. No unrest in facial or cervical muscles; now and again slight fibrillation of the tongue. No dysmasia or dysphagia.

No pareses or rigidity of the extremities; tendon reflexes normal (towards the end of his stay in the ward a tendency to ankle clonus became sometimes apparent). The plantar reflexes were constantly of the flexor type. Abdominal and cremasteric reflexes present.

Stethoscopic findings normal. Pulse regular, though sometimes a little rapid. Liver dulness normal. Urine free from albumin, sugar, bile pigments, urobilin. Blood-sugar (fasting value) 0,084.

Spinal puncture: cells 1/3, globuling 0, albumins 10; Wassermann reaction in blood and spinal fluid negative.

The involuntary muscular movements have all the time occurred in attacks, spontaneously, evoked by muscular action, as, for example, a vigorous "shaking hands", elevation of the arm, and also, by merely calling the patients attention to them; the attack begins by tremor in the right hand in the

¹⁾ This case was demonstrated to the Neurological Society of Copenhagen October 6th 1920 and February 22nd 1922.

form of small, fairly regular, though gradually coarser, flexion-extension jerks at the wrist, slight pro- and supination movements, followed by some bending and stretching jerks at the elbow, some adduction and elevation jerks at the right shoulder, small twitches in the right-sided cervical muscles with tossing of the head towards the left, shoving movements of the trunk, some diffuse muscular unrest (jerks) in the right leg, the trunk being inclined slightly towards the right; eventually, there is a jerking of nearly all the muscles of the body, including the abdominal muscles; sometimes the right arm and the legs will stiffen in the extended position; the left arm is only mechanically shaken by the jerks of the body and right arm.

During voluntary movements the attack increases in intensity; for instance, the movements in the right arm become excessive, choreiform, when the patient shakes hands with anyone.

Face and tongue are not involved in the muscular unrest. The patient remains perfectly conscious throughout the attack; biting of tongue or involuntary micturition never occur. Rather vigorous perspiration and rapid pulse are evident, but no rise in temperature. The attacks have a lytic cessation; their frequency of occurrence varies considerably, two to three attacks, or even more, a day, as also does their duration; in both these respects psychic impressions seem to have some influence. Some days he may be quite free from attacks; he prefers to have a single bed-room.

On the finger-to-nose test his right index finger dashes about in the face; he is unable to keep it on the tip of the nose.

The gait is disturbed by a certain stamping and jerking of the legs; he walks with a rather broad base, now and again with a slight circumduction and dragging of the right foot. During his stay in the hospital, a rather severe static unrest extending all over his body developed when he was in a standing posture.

His state became worse, if anything, up to his discharge January 12th, 1921. After his return to his home the shaking attacks became less frequent but of longer duration, up to 6—7 hours; he is unable to speak during the attacks, and also in the intervals his speech has become more jerky. His handwriting is no longer legible. He suffers from imperative micturition (with occasional soiling).

18th December 1921 he was readmitted: he was perfectly clear of mind, no signs of dementia. Speech difficult, slow, somewhat stumbling, slightly nasal. The tongue is curved, having a marked deviation towards the left; also fibrillating. Otherwise the cranial nerves are intact. No facial muscular unrest. There

are still no pareses in the limbs, but some extension spasticity, brisk tendon reflexes and slight ankle clonus, on the right side; the plantar reflexes are of the flexor type. No disorders of sensibility; no ocular symptoms. The spinal fluid constantly negative. There is trace of urobilin in the urine. There was no rise of temperature, as was also the case during his first stay in the hospital.

When the patient lies completely relaxed in a horizontal position, there is no muscular unrest; but, the slightest muscular action of limbs or trunk, attempt at sitting up in bed, or the like, will often bring on the shaking paroxysms which we have described, which may however also occur spontaneously, and which are now frequently preceded by a severe extension spasticity in the right arm and both legs, having otherwise a course as described above. The contorsion position of the trunk (towards the right) is often extremely pronounced during the attacks, while, in the intervals, it is but slight and easily corrected. The face and the eyes have, as yet, been spared. The left arm, however, is now directly involved, with rapid, clonic elevation jerks in the shoulder, jerks in triceps, while in forearm and finger muscles a muscular unrest is doubtful. Now and again both arms are thrown out into excessive choreatic jerks. During the attacks the respiration becomes somewhat rapid and difficult; there are never any interparoxysmal respiratory disturbances.

His gait becomes more and more miserable, with severe choreatic tottering and swaying movements of the legs, he is hardly able to walk even with support; he can keep standing on his feet, but sways considerably; and at this test, a general shaking of the body is easily provoked. It is remarkable that, at present, he is able to perform the heel-to-knee and finger-to-nose tests with but little unsteadiness.

During his last stay in the hospital (until 21st December 1922) his condition became more and more miserable; he had to be kept as quietly as possible in bed in order to avoid the shaking-paroxysms; he could hardly eat without assistance. Occasionally he had also nocturnal attacks during sleep.

Case 45. Married woman of 44 years, admitted to my department January 4th, 1924. Her grand-mother, two of her mother's sisters, and a cousin, insane. She herself has had periods of depression.

In August 1922 she was taken ill with pains in the right shoulder, spreading rapidly to most of her joints. On September 7th, 1922, she was taken to the Bispebjerg Hospital, of Copenhagen. There her condition was regarded as one of rheumatic

fever, the temperature during the first weeks of her stay showing slight elevations, the pains in nearly all her joints being rather severe, with painful and reduced movements, but without "conspicuous objective signs". There was no pronounced drowsiness, no muscular unrest. Neither ophthalmoscopic examination nor lumbar puncture was made. She had several metrorrhagias; meteorism and pains in the right ileo-cecal region gradually developed, and on February 2nd, 1923, she was transferred to the surgical department, a condition of ileus being supposed. Here she was subjected to an abrasio uteri and subsequent treatment with X-rays; after which her catamenias ceased.

In the ensuing period she has had two more attacks of polyarticular pains, especially in the right-sided joints, accompanied by sensations of fever. During the last three months of 1923 she was treated in the Rigshospital. Here she was depressed, anxious, would frequently weep, but was at the same time "dull" and somewhat somnolent. She slept badly at night, would sometimes leave her bed, appearing to be a little confused. "Shaking of the right arm and the right leg" were noted in the Rigshospital; the head was held a little turned to the right, and there was a painful tension of the left-sided muscles of the neck. Once, she had a lipothymia. The temperature was usually normal except on three evenings, when it rose to 37.8° .

After her discharge from the Rigshospital, December 16th. 1923, her depression has persisted, visual hallucinations, of animals and men, have been very vivid, causing great anxiety, and on the day of her admission to my department she had attempted suicide by gas.

In the ward, she was depressed, not quite orientated, stated that she remembered nothing of what had occurred during her stay in the Rigshospital. No marked somnolence, no true bradyphrenia. The voice markedly bradyphasic, drawling, slightly hesitating, with a nasal tone. The face rather oligomimic, the left angle of the mouth drooping. Usually, the head and the eyes were turned a little to the right. Now and again, a fine nystagmoid lateral jerking of the eyeballs was seen; frequently there was an upwards and outwards squinting in the right eye, but in voluntary movements there were no defects. Size of pupils equal, pupillary reactions, eye grounds, visual fields, normal.

There was a continuous fibrillation of the lips, frequent myoclonic jerks in the muscles of the mouth, of the nose, in the right frontal muscles. Sometimes, the mouth was drawn out in a transverse smile. The tongue fibrillated violently. There

was a continuous, vacillating unrest of the head. In the right arm, which was held slightly adducted and flexed at the elbow, numerous myoclonic jerks were seen, quite small or more coarse, causing slight shrugging movements of the shoulder, extension and flexion jerks in the elbow, slight pronation of the forearm, most varied movements of the fingers and the wrist, the myoclonias being thoroughly asynchronous. In the right thumb a more persistent Parkinsonian tremor was sometimes present. On elevation of the arm or on voluntary action the muscular unrest became very coarse. In the abdominal wall some slight myoclonic jerks might be seen.

The right leg was flexed a little at the hip and the knee, slightly adducted, and here, too, numerous myoclonic jerks or a more continuous shaking of the whole limb was seen, especially in the foot. These myoclonias were neither synchronous in the leg nor with those of the right arm. Neither in the arm nor in the leg were any athetoid, choreiform or torsion-like movements seen.

In the left arm and leg there was absolutely no muscular unrest.

There was a mild hypertonia in the right arm and leg, though no diminution of muscular power. The right knee jerk moderately exaggerated, right-sided ankle clonus, no Babinski sign. No sensory or sphincter troubles. In the spinal fluid were found: cells 0/3, globulins 0, albumins 7. The Wassermann reaction negative both in the blood and the spinal fluid.

The temperature has only once risen to 37.7° in the evening. Gradually, she has developed a slight bradycardia (60 per minute). As to her cardiac attacks, compare p. 26. A close examination of the heart, including X-raying, and of the lungs has not revealed any morbid changes. No abnormal findings in the urine. No affection of the joints.

During her stay in my department she has had three "fits", viz. sudden stiffening of the arms, clenching of fists, strong myoclonic jerkings in the face, in the right-sided extremities as well as in the left leg, whilst there are no jerks in the left arm. During the fits she complains of heavy pains in the back of her neck. There is no loss of consciousness, no biting of tongue, no involuntary micturition. The duration of the fits has been up to a couple of minutes.

She has had an argotropine treatment. The myoclonias have subsided to a considerable extent, the face has become more expressive, the bradyphasia has improved very much, whereas the hypertonia has only been influenced very slightly, especially as regard the leg.

I do not think it necessary, in this case, to enlarge on my diagnosis of chronic epidemic encephalitis. I only want to draw attention to the arthralgic stage of invasion, feigning a "rheumatic fever". As mentioned above (p. 77), the later occurrence of a hyperkinetic condition is, according, for instance, to Mlle Lévy, rather frequent in such cases. It should also be noted, that the abdominal pains, occurring during the patients stay in the Bispebjerg Hospital, suggested the diagnosis of an ileus. Fortunately, the patient escaped a laparotomy.

As to the mental troubles of this patient, viz. the depression, the hallucinations, leading to an attempt at suicide, I should be inclined to suppose them as being due mostly to her maniac depressive constitution, the chronic encephalitis acting in a "mobilizing" way.

Case 46. A woman of 38 years, married; admitted 12th January 1922¹⁾.

Her family history is negative as regards nervous and mental diseases. Up to the present illness she had neither had nervous troubles, nor any other serious physical illness; she denies syphilis, and alcoholism.

In 1917 she was laid up for some days during the severe epidemic of "Spanish disease" (her husband was ill at the same time); there were however no definite cerebral symptoms. "Some time later" (her own and her husband's statements are somewhat vague) she began to experience a sensation of fatigue in the limbs: for short periods her right arm was almost paralysed, afterwards the left. In addition, she had "shaking and sprawling" in the fingers. For a period she often had attacks of giddiness accompanied by a reeling gait. During the last two years her left leg has been "stiff", when walking, and during recent months her left arm has again become affected: „she has not the full use of it", "it does not swing in rhythm, when she walks". The muscular unrest in the fingers and the hands seems to have been very variable (to the point

¹⁾ Demonstrated in the Neur. Society of Copenhagen 22nd Febr. 1922. This patient and those of the Cases 43—44 have also been shown in cinematograms at the meeting of the First Interscandinavian Congress of Neurologists in Copenhagen, August 1922.

of intermissions?) during these years; in the last month, however, it has become more continuous in the right hand. More recently she has had much grimacing in the face: "the eyes will frequently close", etc. Occasionally also some disturbance of speech: "she easily gets short of breath so that she cannot speak properly". There never was true dysphagia, but a sensation, when she is swallowing, as if the throat was "tying itself up into knots". For a period she had "backaches". No headache, vomiting, or visual disturbance. The patient, who seems to be of inferior intellect and of an emotional temperament, has been somewhat depressed during the last four years, with weekly exacerbations, crying and the like, and bad sleep.

She is of a healthy, rustic appearance; intellect rather poor; somewhat erethic. She is mentally clear, but her anamnestic statements are very indefinite. At times, she is rather miserable, though not truly melodramatic.

In her face there is rather monotonous, grimacing unrest, more pronounced on the left side, with forced pinching together of the eyes, violent unrest in the zygomatici, twisting of the mouth, frowning with excessive opening of eyes, etc. Partly, this grimacing is moderately quick, alternating, tic-like, or more choreiform, and partly, it will stiffen in a more stationary "masque de crispation", of some minutes' duration. The facial expression is sometimes piteous, scared, sometimes more clownish.

The kinetic unrest in the arms was at the commencement rather varying: at times the entire arm would stiffen into torsion attitudes (see later); more frequently, however, there was a motor unrest, especially in the fingers, which would move either slowly into athetotic-dissociated positions, or would show medium-rapid choreatic jerks, or, again, slight rhythmic, clonic "raps" on the bedclothes with the closed fingers. There was also a slight quivering unrest without definite motor effect. Occasionally also the arms would be lifted sideways or forwards by rapid choreiform jerks at the shoulders.

At the time of her admission the legs already showed a tendency to stiffening in an extended position but without any pronounced rigidity; the toes were sometimes in a fan-like position, and there were also small clonic jerks.

Now and again the trunk showed a tendency to bending backwards in a light "arc de cercle", more especially simultaneously with the torsion attitude of the arms.

The gait was extremely cautious, the left leg being carried like a stilt; lordotic retroflexion of trunk, walking with eyes nearly closed, at last falling backwards (with incontinence of feces).

To begin with, the spasms as well as the abnormal attitudes, were obviously influenced by diverting the patient's attention, by the presence of the physicians, by voluntary movements, etc. They disappeared during sleep.

The "hysteriform" aspect of the picture was, however, during the further course of her disease, quite overshadowed by the massiveness of the symptoms, both as regards intensity and persistence.

More persistent distortions of the entire trunk gradually appeared (Plate I a—c): usually the head was bent backwards, the neck dug into the pillow, the cervical muscles were highly contracted; the trunk in a varying degree of opisthotonus, and frequently, in addition, varying grades and forms of lateral distortions; the arms, alternately, in rotation-extension-flexion attitudes; the fingers sprawling, athetotic-dissociatedly, in different ways; the legs gradually stiffening in an extended posture, like posts; the left leg being usually lifted slightly from the bed. As a rule the face was set in one or another grotesque "grimace". She had a tendency to bite her underlip so that it bled. On the whole the tongue was quiet. Periodically strong trismus or rhythmic, medium-rapid, loud chattering of the teeth, was evident. The distortions persisted during sleep, but with relaxed muscles.

Also the other forms of kinetic disturbance grew more and more persistent, although, constantly, like the torsion spasms, they were aggravated during the paroxysms. In addition to the more fixed torsion postures there were nearly always slow twisting movements, now more pronounced in the arms, now in the cervical muscles, in the legs, or in the fingers and toes, as typical athetoid movements.

Both the more generalised distortions and the more localised "writhings" increased, however, to a perfect muscular delirium during the paroxysms which, at the commencement, seemed to be provoked by psychic influences; but later, when she had almost constantly a room by herself, they seemed to occur quite spontaneously: the twistings of the trunk and the muscular unrest increased at a fairly rapid rate, she "reared" backwards or doubled herself up, raising the legs and the upper trunk from the bed so that she balanced on the buttocks, the chin pressed firmly on the breast, the facial grimacing culminating, and the arms writhing and turning in the most bizarre contortions. At the same time, there was also severe myoclonic jerking, elevation, adduction of the shoulder, flexion-extension jerks at elbow, hand, fingers, etc.; again, the whole arm would sometimes be thrown laterally or forwards

in a coarse choreatic tossing-movement. The clonic jerks would reach a rate of 120—150 per minute, being, on the whole, rhythmic. In the legs there were flexion-extension jerks with drawing up of the leg to the point of an acute angle. In the abdominal muscles now and again, frequently unilateral, slowly-twisting or more rapid clonic twitches, having almost the character of a rhythmic "dance" of the stomach muscles.

During the paroxysms there is considerable hypertonia in all the muscles of the body; interparoxysmally there is spasmus mobilis. As a rule the distortions could be corrected, only, however, to be quickly reproduced.

During sleep, muscular unrest was never noticed.

The paroxysms were accompanied by excessive perspiration (so that her linen often had to be changed), by irregular, tachypneic breathing, very rapid but regular pulse, but no rise of temperature. Clouding of consciousness or epileptiform symptoms never occurred.

The rate of incidence and duration of the paroxysms eventually increased so that she would lie for from 12 to 24 hours in an attack, with shorter or longer remissions.

Neurological examination, when the paroxysms were not taking place, showed: no definite cranial nerve palsies. Eye-movements free; no nystagmus. Pupillary reactions, eye grounds normal. No corneal pigmentation. No labial or glossal fibrillation or atrophy; no difficulty of chewing or swallowing. The speech now and again somewhat breathless-staccato, becoming somewhat more bradyphasic as the muscular unrest became more pronounced; on a few occasions it became dysphonic during a paroxysm so that she could only whisper. Gradually some pallilalia developed.

Voluntary muscular action of the limbs gradually grew strongly impeded by the torsion postures, though no true pareses set in. The muscle tonus was, as has been indicated, varying; at times perfectly normal.

Tendon reflexes of the arms and legs were present, but could only with difficulty be elicited at a later stage of the disease on account of the muscular unrest, distortions, etc. Clonus was never present. The plantar reflexes were always of the normal flexor type. The abdominal reflexes were absent.

Sensibility was intact throughout; as was also the control of bladder and rectum.

On the finger-to-nose and heel-to-knee tests there was no true ataxia, though the movements were somewhat compromised by muscular unrest (which also seemed to be somewhat increased by voluntary movements). Eventually some static and action tremor set in.

Apart from the paroxysms, there were no distinct respiratory disturbances; on stethoscopic examination strikingly pronounced saccadé respiration was however heard in both infrascapular regions (diaphragma spasm?)¹⁾.

Examination of the heart revealed nothing abnormal beyond strong hammering sounds. Pulse rate somewhat varying, up to 102 a minute, but no more pronounced tachycardia.

Blood pressure 140—150 mm. No palpable peripheral arteriosclerosis.

Blood picture (Leishmann), blood sugar determination gave normal figures.

Hepatic dullness extending from the sixth rib to the curvature. No ascites. Icterus was not observed during her stay in the hospital.

The urine never contained albumin, sugar, or urobilin.

Three spinal punctures showed: cells 0—3/3, globulins 0, albumins 10; Wassermann tests in serum and spinal fluid negative.

During the greater part of her stay in the ward the highest evening temperature was 37,8°. Periodically, however, and without any organic affection being detected, there occurred a hyperthermia of 2—4 days' duration, with temperature up to 38,3°. Subcutaneous injection of 3/4 ccm of the patient's spinal fluid produced a strong hyperthermia (of up to 40,5°) for 11 days²⁾.

Later she suffered from excessive thirst. Her appetite was particularly good throughout, sometimes to the point of greediness; nevertheless, she persistently lost in weight, declining from 61 to 45 kgs. during her seven months' stay in the hospital.

The clinical picture was steadily and excessively progressive; at last the patient lay perfectly helpless in her bed. At an earlier stage she had been slightly clouded for some weeks, somewhat uncleanly, having mild hallucinations of hearing and some nocturnal anxiety. Apart from this she remained clear throughout; no signs of dementia; eventually her condition caused her to be somewhat unhappy. On a few occasions she had fits of spasmodic laughter.

All treatment proved to be ineffective. Her husband took her home August 30th, 1922, and she died in January 1923.

The spinal fluid from this patient produced encephalitis in rabbits (cf. p. 223).

¹⁾ Unfortunately, X-raying was out of the question owing to the muscular unrest.

²⁾ In other of our encephalitic patients this procedure gave no results whatever.

In this patient, too, the extrapyramidal hyperkineses during the first few days of her stay, made so grotesque an impression on the observer as to arouse the suspicion of hysteria. Further development of the disease, however, soon led to the correct diagnosis.

The clinical picture is an almost pure "striatal syndrome", an extremely polymorphous hyperkinesia, in which the athetoid and torsion-spasm component is the dominating feature. Considering the vague anamnestic information as to encephalitis infection, and the patient's age, a more "idiopathic" striatal affection, some form or other of a hepato-lenticular degeneration could, at first, not be excluded; however, in its further development, the clinical picture did not correspond either with Wilson's disease, or with the Westphal-Strümpell pseudosclerosis. With the negative neurological findings, apart from the hyperkinesia, this peculiar clinical picture could, in fact, not be found to fit in with any other cerebral affection than a chronic epidemic encephalitis.

S. K. Wilson, Mourgue, Pierre Marie & Mlle Lévy, and others, have insisted on the partial resemblance between the torsion postures found in encephalitic hyperkinesia, and Sherrington's decerebrated rigidity. In the patient in Case 46 some of the postures assumed during her more severe paroxysms doubtless, to a certain extent, remind the observer of decerebrated rigidity, and the same is true of the child in Case 47. I cannot say, however, that this similarity has appeared to me to be an especially pronounced or striking feature in my patients; and, moreover, the clinical picture resembling decerebrated rigidity has mostly been present in phases, only, alternating with other, quite different contorsions. A priori, it is also hardly likely that a disseminated lesion like that of encephalitis would, frequently, manifest itself in a more pronounced and more persistent "decerebrated rigidity", such as results from a definite experimental cerebral lesion, or from a monocular morbid growth in the posterior cerebral fossa, for instance.



a

b

c

d

e

Plate I.

Case 47. A boy, ten years old; a fosterchild. Admitted to my department April 4th, 1923¹⁾.

Illegitimate child; no Hebrew blood in the family. The mother is said to enjoy good health; the father a drunkard. As far as my information goes, no similar nervous diseases have occurred in his family. He is the first born of two children. No information is available as to the circumstances at his birth. He could walk when he was 16 months old, was cleanly in his 18th month, could speak when 2 years old, though "somewhat indistinctly", and he salivated a good deal. There was no enuresis, noctambulism or eclampsia.

He is said to have been left-handed (from birth?); his gait is said to have been normal up to the onset of the present disease.

Of children's diseases he has had rickets and chicken-pox; no intestinal troubles or jaundice.

He is said to have been an intelligent child but of a somewhat "difficult" temper.

According to his fostermother's statement there has been nothing abnormal about his arms, legs or trunk until his eighth year, i. e. until 1921. In the spring of 1921 he was ill for some months with fever (?), drowsiness, ptosis, dimness of vision; no hyperkinetic symptoms. In February 1922 he was again in bed with a similar, though rather severer attack. Simultaneously all the members of the foster family had "influenza".

His present affection had, however, begun to develop after his illness in 1921. The initial symptoms were trembling of the right hand and flexion spasms of the two ulnar fingers. For a long period he was almost unable to use his right hand for eating, and his handwriting became more and more illegible. About a year ago (i. e. subsequent to the second febrile attack) he began to grow "wry" and become hollow-backed, and some time later, to keep his right leg flexed at hip and knee joints, and walk badly. In the autumn of 1922, according to the fostermother's statement, these conditions were considerably aggravated. At the same period he grew more erethic and suffered from nocturnal fear.

Gradually he developed tremor and jerking in the right arm, more especially at night, sometimes also in the right leg. At night, too, he lay in a distorted attitude.

His speech became somewhat indistinct, last winter it was for a period so "paralysed", that he could not express himself

¹⁾ The case was demonstrated to The Neurological Society of Copenhagen 2nd May 1923.

properly. There was never any difficulty of mastication or swallowing. No true paresis of arms or legs, no convulsions; no squinting or visual disturbances. He has become somewhat emaciated, and he complains occasionally of pains in his arms and knees. His mental faculties do not seem to have suffered.

The disease has been constantly progressive.

He is a rather small, slender boy; height about 124 cm, weight kgs. 22,400. Somewhat pale; hemoglobin (Sahli) 70 %; blood picture (Leishmann) normal figures; differential blood count: neutrophile leucocytes 68 %, lymphocytes 30 %, eosinophiles 2 %.

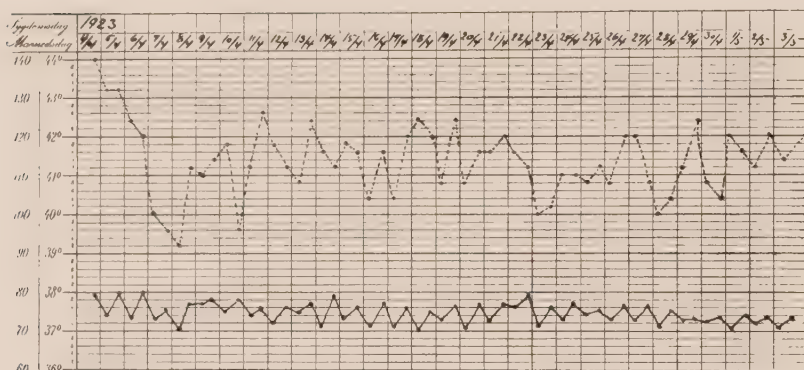


Fig. 32.

No degenerative or dyscrinic-morphological stigmata. No signs of innate syphilis. Hepatic dullness strikingly retracted. No swelling of the spleen. The urine is free from albumin, sugar and urobilin. Diuresis somewhat varying. He is a dys-regulator.

The conditions of temperature and pulse will appear from the curve (Fig. 32), i. e. slightly subfebrile temperatures and a very pronounced tachycardia which persists after the temperature has become normal. Stethoscopic examination of the heart negative.

Only a few drops of fluid were obtained in spinal puncture: cells 1/3, no increase in the albumins at Pandy's test. Bordet-Wassermann test in serum negative.

Psychically the boy is bright, interested in his surroundings, intelligent, perhaps a little precocious; he is a very good and affectionate little fellow; there have been no explosive outbursts of temper, or the like. No disturbances of sleep.

When he stands, the hemitorcion becomes very conspicuous (Figs. 33, 34, 35): his head is turned, chin upward towards the left, his ear almost resting on the strongly elevated (and slightly forward-turned) right shoulder, with extreme hypertonic tension in right sternocleido and trapezius. The entire trunk is twisted towards the right, there is considerable lumbar lordosis. The right arm is kept extended, usually more or less abducted and twisted inwards and backwards at the shoulder-



Fig. 33.

joint, or removed $30-40^{\circ}$ or more from the trunk, frequently slight pro- or supination position of the forearm, wrist usually in maximum volar flexion with slight ulnar deviation, the thumb being as a rule extended and slightly abducted, the other fingers either all flexed to a maximum in against the palm, or only flexed in the metacarpophalangeal joints and extended in the interphalangeal joints.

The right leg is strongly flexed and more or less abducted at the hip-joint, less flexed at the knee, the foot in a fairly pronounced equinus posture, the toes not especially contracted. The entire leg often rotated somewhat inwards. He avoids supporting himself on his right leg, but likes to let the toes

of his right foot rest on the back of left foot, or he balances on one leg. He is just able to stand without support, swaying violently however, falling now and again, now towards the right, now towards the left. If he puts both soles of the feet on the ground, he is only able to stand with the aid of a compensating flexion of the left hip and knee with strong forward-stooping of the body, supporting himself by resting both hands on the right knee¹).

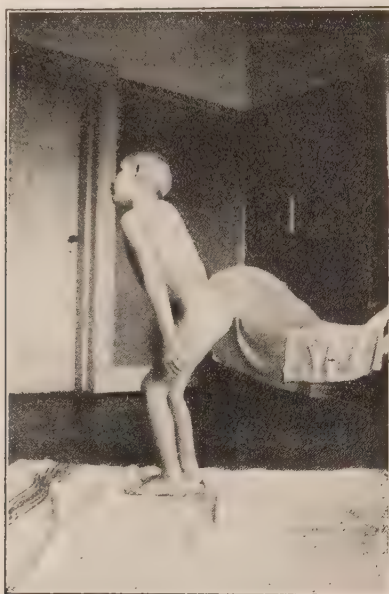


Fig. 34.

He can walk and also jump, with a pronounced "dromedary gait", also here preferring to support the right knee with his hands (Plate I d—e). On letting the right arm go, it will swing out violently sideways during walking.

The distortions grow worse, the more he stands or walks.

In a supine position, also, the marked lordosis, the general twisting of the trunk, and the contracture in right hip, exist. The arm will however approach the trunk in a more natural position. When lying on his back, his head can be moved

¹) Radiography of the right hip and lumbo-sacral region showed nothing abnormal.

fairly freely in all directions; the elevation of the right shoulder can also be fairly well corrected, only to be reproduced shortly afterwards. The lordosis can be corrected, but only by maximum flexion of the right thigh, which however gives rise to a pronounced tonic standing-out of rectus and adductors of the thigh and to light clonic jerks in these muscles. The lordosis is promptly reproduced when the thigh gets into a position of 90° towards the abdomen and is further increased by an attempt at full stretching at the right hip-joint. Correction of the torsion postures of the trunk is only possible to a slight extent. The contracted right hand and fingers permit of redressment; however, the abnormal positions are immediately reproduced.

The tonus of the right-sided muscles is somewhat varying: there is a fairly persistent hypertonia, as mentioned, in the sternocleido and the trapezius, in the deltoid, in the muscles of the upper arm, the flexor group of the forearm, the right-sided long muscles of the back, and the muscles of the right hip and thigh. More especially, on attempt at passive movements the muscular resistance is extremely varying in degree, the same having been the case day by day, so that we have a pronounced spasmus mobilis.

The torsion postures exist during sleep. The intensity of the torsion postures is somewhat varying; the oscillations, however do not manifest themselves as true athetoid movements. Only in the fingers of the right hand, the more continuous contracture will occasionally be replaced by some slow, not quite typical, athetoid flexion and extension movements.

There is no paresis in arms or legs. Right thigh (and right forearm) perhaps slightly thinner than left; there is, however, no distinct hemiaphasia, no localised muscular wasting. The muscles responded normally to electric currents; direct mechanical excitation showed the muscular excitability to be slightly increased everywhere. There was nowhere myotonic after-contraction.

The tendon reflexes could only be elicited with some difficulty in the right arm; in the right leg they were slightly exaggerated, now and again with trace of foot-clonus. The plantar reflexes were most frequently of the pure flexor type: no definite Babinski sign.

In the right side of the face, more especially in the frontalis and at the right angle of the mouth, there were light myoclonic twitches or fine trembling; also fibrillation of the tongue: now and again myoclonic twitches in the various muscles of the right arm and leg, without any marked motor effect; the twitches were not distinctly rhythmic or synchronous. No definite choreiform movements.

No tremor at rest; slight static tremor in the fingers of right hand; no pronounced action tremor. If the stands up for any considerable period, a static tremor of head and trunk will begin.

No abnormal associated movements; no myotonic afterlasting of voluntary movements. Slight ptosis on the right eye, with overaction of right frontal muscle; no other ocular palsies; no nystagmus. Pupillary reactions normal; eye grounds normal. No corneal pigmentation.



Fig. 35.

There is perhaps a slight impairment of the right lower facial muscles. Occasionally the tongue, when protruded, deviates a little towards the left. No palatal palsy. Speech slightly nasal. Mastication and swallowing intact. No respiratory disturbances.

Sensibility intact throughout; no sphincter troubles.

On the whole, his state may be said to have remained almost unaltered during his stay in the hospital. For a short time, the contracture at the hip disappeared, but at present the distortions are rather more pronounced than they were on his admission. Notwithstanding the torsion postures he is exceedingly agile, and hobbles about swiftly in the garden, etc.

The history of this boy fits very nicely into the series of "encephalitic torsion spasms" such as have been described by the above-named authors; its unilateral aspect giving it however a somewhat special feature.

From the point of view of differential diagnosis the only alternative to consider was, in fact, the "essential" progressive infantile torsion spasm (Thomalla, Wimmer)¹⁾.

It cannot be denied that the differential diagnosis may be rather difficult, among other things because it is the localisation of the pathological processes (within the extrapyramidal system), and not at all, or at any rate only to a slight extent, their nature, which determines the symptomatological picture of the disease.

It is therefore to be expected that torsion spasms of a different etiology would give almost identical clinical pictures, and in such cases we can only arrive at a correct diagnosis by a very careful consideration of the mode of development and general aspect of the clinical picture and of all the possible etiological factors.

In the boy above-mentioned, the clinical picture presented a partial resemblance only to the cases recorded by Thomalla, Wimmer, and others. The outstanding feature here was a "hemidystonia" with persistent torsion postures, while the other forms of hyperkinesia were but little pronounced. The development of the affection subsequent to a more acute febrile phase which strikingly reminds one of lethargic encephalitis, would also speak for the diagnosis "encephalitic torsion spasm" as being the most obvious one. Moreover, the slight subfebrile rises in temperature which occurred during his stay in the hospital, and the tachycardia, tend to corroborate this view.

¹⁾ Wimmer: Spasme de torsion progressif infantile. *Revue neur.* 1921. p. 967.

DIAGNOSIS.

The cases of chronic epidemic encephalitis often call for our most accurate diagnostic judgment.

The recognition of the true nature of the disease in question becomes easiest in the, unfortunately relatively rare, cases in which the chronic stage is directly continuous to an acute febrile phase of a "lethargic" type, or when the chronic nervous symptoms set in at a period not too far removed from such an initial febrile phase.

However, as has been mentioned several times, and as our case histories show, in many instances there has only been a more or less vague and common febrile phase, while in several cases no such phase can be traced at all.

The question therefore immediately arises: how much diagnostic value ought we to attach to positive or negative information, respectively, of an initial febrile phase? What should we demand in this respect in order to put forward the diagnosis of chronic epidemic encephalitis?

Of earlier authors, v. Economo advises us to be rather "large" in this respect. Several of our own cases, and numerous cases reported in foreign literature, make the same demand on us. A well-marked lethargic phase is thus an excellent aid in the diagnosis. But, even though no such phase has appeared, even though we can get no information at all as to a febrile initial phase, these nervous cases can, as a rule, be diagnosed, usually with certainty, sometimes only conjectured with more or less probability, on the basis of the general clinical picture, the symptomatology, and the mode of development of the disease.

This diagnosis may, of course, like others, become "a fashion". But, on the other hand, there is no doubt

that we have every reason to be on the alert against such chronic cases of encephalitis which, in the near future, will doubtless prove to be of sadly frequent occurrence. It is a striking fact that, week by week, patients presenting these clinical pictures, are admitted to my department.

And, here, I will take the occasion to point out, that in Denmark fresh sporadic cases of epidemic encephalitis constantly also occur, only in a few instances, however, of a well-marked lethargic type, — of which we have seen a few in our department; more especially, however, cases with a very vague, non-specific, abortive or “ambulatory” initial stage, that is to say corresponding to that vagueness in the symptomatological features which we find so often in infectious diseases “on the decline”. This would seem to indicate that in the time to come, we may expect to be confronted with, not only the “remnant” cases from the extensive epidemics of encephalitis, but also with fresh cases of chronic epidemic encephalitis.

In the preceding pages I have tried to depict, in its broad features, the general clinical picture of the main types of chronic epidemic encephalitis. This general clinical aspect of the case will in many instances decide the differential diagnosis; but in other cases we must have recourse to a more detailed, balancing, symptomatological and clinical analysis of the patient.

The factors which play a part in differential diagnosis between chronic encephalitis and disseminated sclerosis, have been pointed out previously in the discussion of our Cases 32, 33, 34. In addition to the previous history of the disease, a good deal of stress should be laid on the presence or absence of signs from the pyramidal tracts, spastic pareses, clonus, Babinski's sign. For, even though these symptoms may occur, either isolated or in groups, in chronic epidemic encephalitis, it is very seldom that they are found with the constancy, prominence, and generality with which they appear in

disseminated sclerosis, more especially in the more advanced stages of the latter disease. Extrapyramidal rigidity, bradykinesia, and, primarily, extrapyramidal hyperkinesia, practically always suggest a diagnosis of chronic epidemic encephalitis, and not of disseminated sclerosis. The semiological distinction between the tremor found in chronic encephalitis (tremor at rest or on action, static tremor) and the intention tremor found in disseminated sclerosis, may often be used as a guide in diagnosing. A persistent and well-marked nystagmus also more usually belongs to disseminated sclerosis; just as the peculiar "scanning" speech is but seldom found in chronic encephalitis. As to the absence of abdominal reflexes, which in the opinion of German authors supports the diagnosis of disseminated sclerosis, I dare not, so far as my experience goes, attach to this sign any important differential-diagnostic value. Retrobulbar neuritis optica, other affections of the optic nerve causing central scotomata or sector-shaped defects of the visual field, temporal pallor of the optic discs, should, in doubtful cases, suggest disseminated sclerosis; even though similar symptoms are sometimes met with in chronic encephalitis (p. 66). On the other hand, disturbances of the pupillary reactions, more especially perhaps of the accommodation reaction, almost invariably supports a diagnosis of "chronic encephalitis", provided, of course, that a syphilitic infection can be excluded. Pathological findings in the spinal fluid may be seen in either disease; though whether these are more frequent and more well-marked in chronic encephalitis, I dare not say for certain, but I have formed that impression¹). Again, episodic or pe-

¹) According to I. B. Ayer & H. E. Forster (*Arch. of neur. & psych.* 1922, Vol. 8. p. 31) a mild pleocytosis and a slight trace of hyperglobinosis will frequently be found in disseminated sclerosis, more especially in the progressive and exacerbating forms. In an investigation, carried out in my department, on 50 patients, Dr. Kn. Krabbe found normal figures for the cells in the spinal fluid in 40 %, slight or very doubtful pleocytosis in 40 % and only in 10 % figures up to 8—12 cells.

riodic hyperthermia, and tachycardia, would indicate chronic encephalitis.

Cerebrospinal syphilis is also, in the majority of cases, a disseminated, multilocular affection of the central nervous system, and it must therefore, of course, be involved in our differential-diagnostic consideration, at any rate in all adult cases. The decisive factors, here, will be the previous history of the case, and the formula for the humoral syndrome, i. e. the cell changes and hyper-albuminosis in the spinal fluid, and the presence of a positive Wassermann reaction in spinal fluid and blood. We cannot, of course, exclude the possibility of a person with a syphilitic infection developing an epidemic encephalitis, as might probably be supposed in my Case 42. But, practically speaking, changes in the spinal fluid in connection with a positive Wassermann test, primarily in the spinal fluid, will nearly always indicate a syphilitic affection. As to an isolated positive Wassermann reaction in the blood, only, I should not attach a decisive diagnostic value to it. Thus, a married woman of 27 years quite recently came to my department with a history of a syphilitic infection 6 years ago. 4 years ago, she had the "spanish disease", being very ill for some months, but remembering nothing more special of her symptoms. Some time later she got most classic epileptic seizures, sometimes of a more Jacksonian, rightsided type. In the ward, too, she had two such fits, with complete loss of consciousness, cyanosis, biting of the tongue, tonic and clonic spasms, of minutelong duration, followed by blurred consciousness for some twenty minutes and complete amnesia for the fit. No postparoxysmal palsies. Outside the fits there was found strong fibrillation of the lips and the tongue, swift myoclonic jerks in the muscles of the mouth and the chin, in the pronator and supinator muscles of the left arm, in the right foot, whilst there was a moderate static tremor of the left arm and hand and of the left leg. No parkinsonism, no eye symptoms, no disturbances of re-

flexes. In the spinal fluid was found 0/3 cells, 0 globulins, 8 albumins. The Wassermann reaction was negative in the spinal fluid, whereas in the blood a moderate positive reaction was found (0—0—20—100, according to the technic of our Serum Institute). Yet, I should think that the total clinical picture would decide in favour of a diagnosis of epidemic encephalitis.

Most difficult to diagnosis are the cases of pure syphilitic endarteritis of the small cortical vessels, in which the humoral syndrome for a long period, or perhaps even permanently, remains negative. So far as my experience goes, however, the clinical pictures presented by such cases are in all essentials different from those of chronic encephalitis. The pure syphilitic endarteritis, the one which is not to any special degree complicated with syphilitic meningitis, is most usually localised in the brain, first and foremost to the cerebral cortex, manifesting itself by a number of atypical psychotic symptoms and by neurological signs chiefly of a cortical and focal nature: aphasic, apraxic, agnostic, epileptiform, perhaps hemilateral (Jacksonian) seizures, etc.¹). Even though one may meet with extrapyramidal hyperkinesias, for instance, hemilateral movements (Lhermitte, Wimmer, and others), such symptoms almost always indicate an encephalitic, non-syphilitic, affection.

The clinical aspect of chronic encephalitis will not easily be confounded with that of a brain tumor, at any rate not if the patient be observed for any length of time. The previous history; the general cerebral symptoms, which, eventually, at any rate, become very prominent; a well-marked and progressive papillary stasis or an optic neuritis; the constancy and uniformity with which the symptoms develop in brain tumor, as opposed to the more remittent and exacerbating, polymorphous clinical picture of chronic encephalitis; again, the "disseminated" symptomatology of the latter as

¹) Jacob: *Zeitschr. f. ges. Neur. & Psych.* 1920 vol. 54 p. 39; Lhermitte. *L'Encéphale* 1921 No. 1 p. 33.

opposed to the always more monocular and focal syndrome of brain tumor, — all these factors as well as some others (findings by X-raying and, perhaps, by Dandy's encephalography), will, mostly, enable us to make the differential diagnosis.

The extrapyramidal syndrome, the hypertonic-akinetic (parkinsonism) as well as the hyperkinetic one, the abnormal involuntary movements, belong primarily to the clinical picture of encephalitis, and are very rarely seen, at any rate not in any pronounced form, in brain tumor. It should be mentioned, however, that Parkinsonian-like clinical pictures have been seen, for instance, in cases with frontal tumors¹⁾. Such cases are however rare, and in those which have been reported, symptoms (like papillary stasis, etc.) leading to a correct diagnosing, soon became evident.

There are some cases, however, which to a greater extent may present diagnostic difficulties: thus, at my hospital, we have lately been confronted, on several occasions, with diffuse infiltrating, rapidly growing gliomata or gliosarcomata which, without any protracted initial stage, or, at any rate, with but vague prodromes, acutely or subacutely, have given rise to marked cerebral signs, such as anisocoria, associated ocular palsies, vague and transient facial palsies, or paralyzes of the limbs with an inconstant Babinski sign; in one case, again, speech disturbance of a bulbar character, in another mild amyostatic troubles (tremor at rest, shaking on action). In addition, there was fever, in one case up to 39,4° C., and lethargy. The course showed strikingly deep remissions, with afebrile phases, psychic clearing up, etc. In both these cases there was papillary stasis, either on admission, or setting in during the first or second week. On the other hand, however, the pleocytosis (of up to 28

¹⁾ Schuster. *Zeitschr. f. ges. Neur. & Psych.* 1922. Bd. 77, p. 1. In a case recorded by Bouttier, Girot & Mlle Wertheimer, there was a persistent hypertension of head and neck muscles reminding of "decerebrated rigidity" (*Rev. neur.* 1923. p. 754).

cells per ccm) found in the spinal fluid was a confusing factor (there was no hyperalbuminosis, and the Wassermann tests were negative).

In such doubtful cases one ought, perhaps, to attach more importance to the papillary stasis than to the findings in the spinal fluid. But, again, cases like our Cases 29 and 30, deprive the changes in the optic nerve of some of their diagnostic value.

What may also happen is that a chronic encephalitis of a chiefly "bulbar" character, may for a time suggest a cerebello-pontine angle tumor or, again, cerebello-amyostatic symptoms may urge us to consider the possibility of a cerebellar growth.

The differentiation between epidemic encephalitis and cerebral abscess (otogenic, pulmogenic, traumatic, etc.) has been rather exhaustively dealt with by F. Stern. Confusion is apt to occur, however, especially between a cerebral abscess of an acute or subacute nature, and an epidemic encephalitis of a corresponding type. The clinical picture of chronic encephalitis will, however, in all essentials differ very much from that of a cerebral abscess, the symptoms being in the latter case of a more focal nature (sensory aphasia in temporal abscess, severe cerebellar signs in abscesses in the cerebellum, persistent hemiplegias, etc.). The presence of extrapyramidal syndromes, parkinsonism, hyperkinesia, would in these cases decisively suggest a diagnosis of chronic encephalitis. The temperature curve, the findings in the spinal fluid, (if the pleocytosis is not purely or predominantly leucocytic) are, as will be easily understood, of less diagnostic value; as is also a pre-existing ear affection (Cases 15, 18).

The Strümpell-Leichtenstern influenza encephalitis is a hemorrhagic, predominantly cortical inflammation, must usually manifesting focal symptoms, such as hemiplegia, sometimes combined with aphasia, occasionally Jacksonian seizures, etc. The nervous symptoms are either regressive or may remain constant, but without the addition of other neurological symptoms, such

as usually occur in chronic encephalitis. In cases where a so-called "influenza" leaves behind, for years to come, well-marked nervous or psychic disturbances, where more or less transitory neurological symptoms persist, more especially myoclonias, one should, as far as our experience goes, look with great scepticism upon the diagnosis "influenza"; compare our cases in which this diagnosis often figures in the past history.

"Serous meningitis" is as yet so vague a nosological term, and we are so ignorant as to its etiology, that it would not seem surprising if several cases of this kind, e. g. certain cases of "pseudo-tumor cerebri", would in the future disclose themselves as being acute or more chronic cases of encephalitis.

In a recent paper, Percival Bailey has surveyed the anatomical findings in the hitherto published cases of "pseudotumor cerebri"¹⁾. In quite a number of these cases some sort of "inflammatory" brain changes were found. In the case reported by Percival Bailey, too, the histological findings in the brain are labelled as a "combination of interstitial and parenchymatous changes". One would not venture to dispute the diagnosis of a case so minutely examined as that of Percival Bailey. Yet, from my knowledge of the pathology of chronic encephalitis, I do not feel quite convinced that, in this case, "the presence of antemortem hemorrhages, the lack of intensive perivascular infiltrations and the absence of lesions in the substantia nigra" are sufficient to rule out a chronic epidemic encephalitis.

Cerebral arteriosclerosis may, as other disseminated encephalopathies, occasionally give rise to diagnostic difficulties. From a purely empirical and statistical point of view, one should be cautious in diagnosing cases of above sixty years of age as "chronic epidemic encephalitis", more especially when the arterial hypertension, the palpable arteriosclerosis, and the renal and

¹⁾ Archives of neur. & psych. 1920 vol. 8. p. 401.

cardiac symptoms are very conspicuous as well as when the symptoms are more focal, persistent, or apoplectiform (massive hemiplegias, aphasic, apraxic, agnostic disturbances, etc.). We must not forget, however, that an old arteriosclerotic patient may become an epidemic encephalitis, which will then add its symptoms to those existing and due to the arteriosclerosis.

Extrapyramidal syndromes may most certainly be seen in cerebral arteriosclerosis, especially in the "lacunaires"¹⁾. But during recent years, i. e. after our great epidemics of encephalitis, I have seen in my ward quite a number of aged persons with marked arteriosclerosis, presenting, besides, some extrapyramidal syndromes, such as hemirigidity, tremor, myoclonias, etc., coming on rather suddenly and accompanied by more or less pronounced hyperthermia. For the most part, these symptoms have passed off after a few weeks. Also, in a few cases, where death ensued, histological changes of a true encephalitic nature were found in the brain together with arteriosclerotic lesions. These investigations are still being carried on by Dr. Neel in the Psychiatric Laboratory.

When dealing with encephalitic parkinsonism we emphasised the strong resemblance it might bear to the classical paralysis agitans, Parkinson's disease.

According to Pierre Marie & Mlle Lévy, Sicard, Lhermitte, Stern, and others, the following factors should be considered in the differentiation between the two diseases concerned: age, (only 10 of Mlle Lévy's 129 encephalitic cases were above 50 years, the majority below 40); past history: whether there has been an acute, febrile, and, if so, lethargic, initial phase, or not; further, the combination and mode of onset of the symptoms; and, finally, certain semiological minor features which have already been mentioned in the chapter on parkinsonism. Especial importance should be attached to certain forms of tremor (action and static tremors), "cataleptic" signs,

¹⁾ J. Lhermitte: Les syndromes anatomo-cliniques du corps strié chez le vieillard: *Rev. neur.* 1922, 406.

pyramidal tract signs, isolated Babinski sign, ocular palsies, pupillary anomalies, and, finally, myoclonic, choreatic, and athetoid hyperkinesias. If there are any pathological findings in the spinal fluid this would suggest encephalitic parkinsonism; as also would rises in temperature (as in Meggendorfer's, and my own cases), tachycardia, and the like symptoms.

Most of our cases of parkinsonism were, as has been mentioned before, not "pure", but complicated with symptoms that do not belong to the "classic" paralysis agitans. However, as has also been pointed out in an earlier chapter, we may meet with cases of encephalitic parkinsonism which are of the "pure" type. If such cases are, moreover, "cryptogenetic", and occur in individuals of a somewhat advanced age (Case 63), the differential diagnosis may be difficult enough. And, here, we cannot quite dismiss the supposition advanced by Souques, Netter, Mingazzini, and others, that the "classic" paralysis agitans may be, often or perhaps usually is, of an encephalitic origin.

That the heaped appearance of the Parkinsonian syndrome, such as we have witnessed it in the recent years, should contradict the "identity hypothesis" advanced by Souques, as Stern for instance thinks that it does, is hardly tenable.

The far less frequent occurrence of this clinical type in previous times might merely indicate that epidemic encephalitis at that time occurred sporadically only, as it does now after the great epidemics. A case of Souques' is suggestive in this connection: a woman of fifty-two, with a typical paralysis agitans of twelve years standing, which had been preceded by amblyopia and a well-marked lethargic phase lasting for years¹⁾. Netter records a case of a young man with encephalitic parkinsonism, whose father had suffered from paralysis agitans; in both father and son a somnolent period of about ten

¹⁾ *Revue neur.* 1922 p. 304.

days had preceded these illnesses¹⁾. An observation such as the following might be used to bear out the same hypothesis.

Case 48. A woman, aged 38, admitted to my department 3d March 1923. In 1909 and 1911 she had "influenza", i. e. a week's fever, marked somnolence, deliriums, as well as some mild ocular symptoms. Subsequently, she enjoyed fair health until



Fig. 36.

about three years ago; it is noticeable that she had no febrile or lethargic attacks whatever during the periods of our great epidemics in Denmark (1919—1920). She began now to suffer from palpitation, dyspnea, dizziness, loss of hair, emaciation; no menstrual disturbance. During the past year, moreover, trembling of arms and legs when working, though not when at rest. There were no other hyperkinetic symptoms.

She is poorly nourished, somewhat presenile; blood pressure 110 mm; she has a fairly marked mask-like face, and Parkins-

¹⁾ *Revue neur.* 1921 p. 574.

onian attitude (Fig. 36); also some salivation; she is rather bradykinetic and bradybasic; no antero- or retropulsion. There is no pronounced rigidity; she shows a tendency to stop half way in active movements of arms, and to remain stationary in fixed positions; there is suggestive catalepsy. Medium fine, medium rapid rhythmic tremor at rest in the fingers, most marked on the right side, aggravated when the arms are elevated, though not by action which, on the other hand, does not lessen the tremor.

No symptoms from the pyramidal tracts beyond some slight profound hyperreflexia. No ocular symptoms except for some impairment of convergence movements.

The temperature curve is "flat", but there is no hyperthermia; now and again, however, for 2 or 3 days, phases of tachycardia occur, the pulse rate rising to 100 beats a minute. No pathologic findings in the urine. Spinal puncture showed: cells 0/3, globulins 0, albumins 7; Wassermann tests negative in serum and cerebrospinal fluid.

If, in this case, we had not had our attention focussed on the possibility of an infectious etiology for her "paralysis agitans", we should most probably not have obtained any information as to the attacks of "influenza" with somnolence in 1909 and 1911. It cannot, of course, be established with absolute certainty that the present illness of the patient has any etiological connection with these febrile attacks. Her past history, however, does not supply us with any other likely cause. Besides her age, the absence of a palpable arteriosclerosis or arterial hypertension is against the usual presenile paralysis agitans.

Supposing an infectious genesis for her present illness, it seems to me far more natural to go back to the reliable infectious phases in 1909 and 1911, than, for instance, to "interpolate" an encephalitic infection from the more recent epidemics; this would be quite arbitrary.

As far as our knowledge goes at present, it is not easy to take up a standpoint in regard to 'Souques' "identity hypothesis". It may be that the encephalitis virus is merely one of the (infectious) noxæ which, perhaps combined with an "abiotrophic" disposition in the cerebral areas concerned, primarily the substantia

nigra and globus pallidus, will gradually give rise to the regressive changes manifesting themselves in the clinical type known as paralysis agitans (Parkinson's disease), the patho-histology of which in essential points (more especially as regards the perivascularitis) differs from that of the chronic encephalitis (François & Lhermitte, Lhermitte & Cornil¹), Marinesco, König, Meggendorfer, F. H. Lewy²). It must be admitted however, as Souques also points out, that our knowledge of the etiology of Parkinson's disease is, for the present, extremely deficient, and that, for instance, the doctrine of the presenile or senile "abiotrophy" is in itself just as hypothetical as is Souques' identity theory.

In the preceding pages we have occasionally hinted at the points of resemblance existing between certain forms of chronic epidemic encephalitis and the "hepato-lenticular degeneration" (H. C. Hall), Wilson's disease, the pseudosclerosis of Westphal-Strümpell, and certain forms of "torsion spasm" (Thomalla, Wimmer). The past history, the mode of onset and development of the disease, the grouping of the symptoms, will in these cases be decisive factors in the differential diagnosis. The hepatic affection which, although not with absolute constancy³), is found in the "hepato-lenticular degeneration", unfortunately only rarely manifests itself clinically *intra vitam*. The presence of a "corneal ring" is positively against the diagnosis chronic encephalitis.

¹) In the case reported by these authors, epidemic encephalitis in a patient with true paralysis agitans, the pathological changes peculiar to encephalitis (i. e. perivascular lymphocytic infiltrations) were found side by side with the regressive changes in the ganglion cells and the neuroglia (within the frontal lobes, globus pallidus, locus niger), which are usually regarded as being characteristic of "classic" paralysis agitans (*Revue neur.* 1922 p. 428).

²) F. H. Lewy: *Die Lehre vom Tonus und der Bewegung*. Berlin 1923, p. 599.

³) Wimmer: *Pseudo-sclérose sans affection hépatique*. *Revue neur.* 1921 p. 1207.

Neither Stern, nor I, myself, ever found it in encephalitic patients ¹⁾.

Where the motor restlessness in encephalitis is more of the purely choreatic type, it will often bear a strong resemblance to Sydenham's chorea or Huntington's disease. There is, therefore, every reason in the future to consider a diagnosis of chronic epidemic encephalitis in cases of "arhythmic" chorea (Mlle Lévy) of an uncertain etiology. Present evidence suggests our regarding Sydenham's disease, too, as having an infectious origin. Its underlying pathological changes are inflammatory foci in the brain, especially in the cortex and the basal ganglia ²⁾. Chorea minor also shows a marked tendency to recur, thus corresponding in its course to that of chronic epidemic encephalitis with its relapses. In certain cases the relapses coincide with pregnancy, a fact also found sometimes in chronic encephalitis.

There does not seem to me to be any decisive semiological distinction between the motor restlessness found in encephalitic chorea and that of Sydenham's chorea. The differential diagnosis must therefore be based on other factors, such as the past history (rheumatic fever, scarlatina, angina, etc.), the endocarditis, the pure choreatic restlessness without any addition of other nervous symptoms such as ocular signs, rigidity, tremor, myoclonia, Babinski reflex, and the like.

Case 49. A man of 22 came under my care December 29th, 1923. Previously healthy, he became ill in October 1916, and was for half a year treated in a country hospital for "nervousness". The medical reports state that he had continuous jerks of the shoulders, tossing of the arms, and that he would pinch himself in the chest with the left hand. Frequently there were rises of temperature up to 38°. No eye symptoms, no respiratory

¹⁾ Yet, Holzer, Westphal & Sioli (Arch. f. Psych. u. Nkhd. 1922. Bd. 66 p. 747) have published cases indicative of possibly transitional affections.

²⁾ Pierre Marie & Trétiakoff: Rev. neur. 1920 p. 428; Greenfield & Wolfson: The Lancet 1922. II. p. 603.

troubles, no drowsiness. After his discharge from the hospital, the jerks persisted, he kept on "pinching" his chest, thus producing a rather extensive excoriation beneath the left papilla. He complained of unpleasant paresthesias in this region. He would often sigh deeply, or groan, while occasionally some twitching of facial muscles could be seen.

His condition remained rather stationary until the autumn 1923, when the jerks grew more frequent. He developed headache, giddiness, apathy, weariness, dyssomnia.

In the ward he showed a noticeable motor unrest. Grimacing movements were noticed in the face, or more isolated myoclonic jerks in different muscles. The arms were sometimes tossed about in rapid choreatic jerks, or he would "beat" or "pinch" himself on the chest. Or, again, true myoclonic jerks would appear in various muscles of the arms, frequently in series of 10—20. Now and again, the abdominal wall was agitated by rapid side-jerks, the breathing becoming a little staccato, and very frequently he would "groan" for some time. In the feet, too, some rare extension jerks might be observed. On occasions he had a little difficulty in beginning to speak.

Doubtless, his motor unrest was largely influenced by the medical examination, in the presence of his visitors, etc., on one occasion developing into a hysteriform "fit".

No hysterical stigmata could be found. He had a feeling of weakness of the left arm and leg, but there was no true paresis. The type of the left plantar reflex was a little dubious. No change of muscular tonus. Movements of eyes, eye grounds, pupillary reactions, fields of vision, normal. Spinal fluid showed 3/3 cells, 0 globulins, 6 albumins. Wassermann test normal in blood and spinal fluid. For the first 12 days of his stay, he was feverish, the temperature reaching 38.2° in the evenings. The rate of the pulse from 68 to 100; no irregularity; no abnormal findings in the heart.

Mentally, he is rather defective; somewhat imbecile, querulous, meddle some, will sometimes scold those around him, tear his clothes to pieces, etc.

The fact that the febrile phase preceding the present illness, occurred in 1916, that is before the outbreak of the great epidemics of encephalitis in this country (1918), does not, in my opinion, exclude a diagnosis of chronic epidemic encephalitis. At least, the clinical picture is not at all that of the classic chorea of Sydenham, nor does the patient present any affection of the heart, etc.

The supposition, that the case is merely one of "hysterical chorea", seems to me so far-fetched, that I do not think it necessary to undertake any advocacy against it.

When differentiating chronic encephalitis from Huntington's chorea, other factors again, such as heredity and familial occurrence, respectively, as well as dementia, will be contributory.

Yet, sometimes, a history of similar diseases in the family may not exclude the presence of chronic epidemic encephalitis.

Case 50. Thus, some time ago, a married woman of 26 came to see me in my private practice. Her mother and her sister had "St. Vitus's dance", whereas her three elder brothers and a younger sister were perfectly healthy. She, herself had been in good health up to 1919, when she was taken ill with fever (up to 40°), pronounced somnolence, nocturnal delirium, though no eye symptoms or involuntary muscular unrest were observed. She stayed in bed for about three weeks, did not quite recover, and, about six months later, she had another attack quite similar to the first, though of diminished intensity, lasting a week. Then, again, in 1920, she had a third attack of the same kind of some days' duration. After that she felt perfectly well, showing no signs whatever of epidemic encephalitis, until the spring of 1923, when she developed a rapidly increasing drowsiness and apathy. She would sit for hours quite passive in a chair, seemingly paying no attention at all to what was happening in the house, could not speak spontaneously, seemed to overhear questions addressed to her, would sometimes let the baby drop out of her arms, etc. Her movements, her gait, and her speech became very languid. She, herself, declares that everything that occurs "passes before her eyes", she does not realise what is taking place, she no longer possesses any interest in what is happening'. Her memory has become exceedingly bad, she lives in a fog, will put her things in the most extraordinary places, being quite unable to find them again. Her memory of the period previous to her illness is not impaired. She has become rather depressed over her condition, and often cries; there is no dyssomnia.

Together with the psychotic symptoms, myoclonic or slightly choreiform grimacing jerks in the lips have appeared, in the fingers and hands, sometimes also in the toes and feet, small, quick, intermittent, isolated jerks, not synchronous. In the left vastus femoris a more continuous fibrillation is seen.

She is somewhat obese; no signs of myxoedema. No paresis, no marked Parkinsonian carriage, no hypertonia. Tendon reflexes brisk; no clonus, no Babinski sign. No troubles of cutaneous sensibility. Left pupil reacts very sluggishly to light; the accommodation reaction, too, is a little diminished. No impairment of eye movements.

She is rather bradyphrenic, but there are no real defects of intelligence.

As early as 1901 Babinski suggested that certain organic alterations of the brain, primarily localised in the basal ganglia, might be the cause of certain tics, more especially of the spasmodic wry-neck¹⁾.

Our experience in regard to the encephalitic "sequels" to a great extent bears out this theory, a theory which has later been advanced also by a number of other authors: Pierre Marie & Mlle Lévy, Babinski, Long-Landry, André Thomas & Mlle Meige, Tinel, Higier³⁾, Cassirer, Bostroem, Foerster⁴⁾, R. Bing, etc. In cases where the "tics" occur monosymptomatically, without concomitant nervous symptoms of any other kind, and without an infection being reliably evidenced in the anamnesis, we should of course be cautious of immediately suspecting "an encephalitic sequel". On the other hand, however, too many such cases have no doubt previously been classed in the categories of "tic mental" or "hysteria". Even true hysterical symptoms need not here mean anything but an "overlapping" hysteria, a "hystérie surajoutée". In the future we shall no doubt gain a good deal of information in regard to this point.

One of my patients presented a peculiar diagnostic difficulty in that he, in addition to an encephalitis, suffered from hereditary tremor in the hands. His history is of interest also on another account, namely the appearance of an "ambulatory automatism".

¹⁾ Exposé des travaux scientifiques. Paris 1913. p. 178.

²⁾ Revue neur. 1922 p. 288.

³⁾ Deutsche med. Wochenschr. 1922 p. 1276.

⁴⁾ Zeitschr. f. ges. Neur. u. Psych. 1921 Bd. 73. p. 1.

Case 51. The patient was by occupation a fireman, aged 48, admitted to my department 20th October 1923. His father's father, his father, and two brothers suffered from hereditary tremor, whereas his three sisters were all spared this infliction. He himself had from his earliest childhood suffered from tremor of the hands in action, to such a degree that he had not even learned to write nicely. In childhood he was a somnambulist, and continues to be so still. Apart from this there have been no previous neurotic or hysterical attacks. Moderate use of alcohol. Prior to his present illness he had never convulsions, absences of mind, other episodic troubles of consciousness, fugues, or the like. He is of a well-balanced temper.

Three years ago, the patient had the "Spanish disease", the temperature rising to 41° ; he was extremely somnolent for about four weeks, but there were no definite mesencephalic symptoms. After his illness not only was the tremor in the hands aggravated during action, but there was now also tremor in the fingers at rest, more especially in his left hand, sometimes increasing to coarser shaking of the arms, more especially when he grew hot or excited. He has been troubled a great deal in his work by these symptoms. After his illness he has had to use spectacles when reading, whereas his vision is still good for long distances. His libido has completely disappeared. There is rather excessive loss of hair. No polyuria, no polydipsia, no remarkable increase in weight. Now and again a feeling as if he was going to swoon. He often sleeps badly. There are no general psychotic changes, especially no impairment of memory. No febrile episodes.

About 18 months ago he experienced burning pains "inside" both thighs; during the past year he has had darting pains in the forehead. About a month ago he began to feel that the power in his left arm and leg had become reduced; on standing up too long, his left leg began to tremble.

About three weeks ago he left his home one morning to go on duty at the fire station; he did not however arrive there, nor did he return home until a week afterwards, tired and somewhat miserable; he had almost complete amnesia regarding what had happened during these eight days; the only thing he could remember was that, at a certain time, he had been in one of the suburbs of Copenhagen, but then he had "lost memory again"; at last he had "come round" and had found himself sitting on a bench in one of the boulevards. He believes that he must have spent the nights in the open; he had some money with him when he left his home, and he had used some of it (for food?). There were no signs indicating that he had had

a seizure, and he had not been in for any alcoholic debauché prior to this fugue. No return of memory in regard to the happenings of this period has occurred, neither has he suffered from any further attack of this sort.

Patient is a well-developed, somewhat stout man; face slightly flushed, somewhat oligomimic. There is no well-marked bradykinesia or bradyphasia. Some fibrillation of the tongue, slight fine lateral tremor of the raised head, and well-marked Parkinsonian tremor in the thumb of left hand when resting.

In the elevated hands and arms there are coarse arrhythmical trembling jerks, the rhythmic tremor of left thumb persisting synchronously, becoming a little more coarse perhaps. In the elevated left leg there is some irregular side-jerking of the foot. Fairly marked irregular shaking in arms and legs in voluntary movements. Occasionally myocloniform jerks in the muscles of right forearm and some playing with the fingers at rest.

No hypertonia. Power of left arm and leg perhaps slightly reduced. The tendon reflexes are all somewhat exaggerated; there is no Babinski sign. No disorders of sensibility or sphincter control. His gait is perhaps on a somewhat broad base, in fact rather "solemn". Eye movements, visual fields, eye grounds, normal. The pupillary reaction to light is well preserved, on accommodation it "corresponds to the age" (ophthalmologic department); visual acuity 5/6 in both eyes, with + 2.00 and + 2.50, respectively. The hepatic dulness does not extend below the curvature, nor can other signs of chronic alcoholism be found. The urine is normal. The temperature curve "flat", between 37 and 37.4°. Pulse rate rather slow, down to 60. Blood pressure 120; no palpable arteriosclerosis. Spinal fluid: cells 0—1/3, globulins 0, albumins 11, Wassermann reaction in serum and spinal fluid negative.

Psychically there is nothing remarkable about him, there is especially no marked bradyphrenia or failure of memory. No episodic trouble of consciousness observed in the ward; nor somnambulism, seizures, enuresis, or the like.

Presumably this history presents sufficient data for the diagnosis "chronic epidemic encephalitis". Peculiar to the case is the strange mixture of motor unrest, hyperkinesia, myastasia, on the one hand, belonging to the encephalitis, and, on the other hand, the patient's habitual tremor. One feels tempted to regard the amnesic fugue in which the encephalitis in this case manifested itself, as a "mobilisation" of the patient's habitual ten-

dency to "automatism", as displayed in his habitual somnambulism.

As has been mentioned on several occasions in the preceding pages, symptoms with a "functional" character — "neurastheniform" or "hysteriform" — are of no infrequent occurrence as components in the clinical pictures of chronic encephalitis. In some cases such symptoms will even dominate the picture: asthenia, failure of memory, emotional erethism, anxiety, headache, vertigo, pains, sleep disturbances, diurnal somnolence ("lethargies"), oscillations in body weight, cardiac attacks, etc.

There is of course nothing to prevent a "simple" neurasthenia or psychasthenia, toxic, nutritive, or other, following upon an encephalitic infection as well as upon other infectious diseases. Nor can it be excluded that such patients prior to the encephalitic infection may have been psychopathics, chronic neurasthenics or hystericals, the infection thus only accentuating the pre-existing symptoms, a possibility which has been pointed out also by Meggendorfer. In one of my patients, a woman of 44, the anamnesis showed hysterical accidents (mogi-graphia, hysterical motor and sensory paraparesis). Her encephalitic "neurasthenia" was accompanied by pleocytosis spinalis (14/3 cells), alternating nystagmus, and Babinski sign. In such cases, then, and more especially in the cases in which the past history of the patient is purely negative in regard to nervous and psychopathic accidents, the sadly numerous experiences of recent years teach us that there is every reason to be on our guard, and most carefully to follow these patients in their further course; to see that they are re-examined; to have our attention focussed, for instance, on spontaneous oscillations in their body weight, on any dyscrinal symptom, possible episodic rises in temperature, episodic or persistent pulse anomalies, transitory visual disturbances, excessive fatigue and muscular lassitude, slight myoclonic jerks, tremor, and the like. If possible, a lumbar puncture should always be carried out, in

such cases. The myoclonic paroxysms, especially, may in a perfunctory examination easily be mistaken for functional attacks of anxiety, and so on. There may be reason to call attention also to the encephalitic tachycardia and bradycardia, respectively, which might perhaps be confounded with a "neurosis cordis", if a thorough neurological examination is not made. Subjective symptoms, such as violent palpitation of the heart, precordial pains (in paroxysms, Reys), dyspnoea following on exertion, etc., may also sometimes add to the possibility of diagnostic errors.

That true hysterical (psychogenic) accidents — severe crises etc. — may occasionally occur, as has been mentioned by Tinel, Staehelin, and others, goes without saying, these symptoms either overlapping true encephalitic symptoms or being an "auto-imitation" of such previously existing symptoms¹⁾, or, again, occurring in the form of an "association morbide", as seen in the following case.

Case 52. Male, aged 23, admitted to my department May-July 1922. Previously of good health, psychically nothing remarkable; he had "Spanish disease" in 1918, fever, drowsiness, no mesencephalic signs; the attack lasted about a fortnight. In 1919, another attack of fever lasting a few days, but otherwise no definite neurologic or psychotic signs; he was able to earn his living as a sailor and to undergo his period of conscriptive service in the navy. In 1919 his boat was torpedoed and he was washed about for four hours in the sea. After this he grew somewhat "nervous", but not until the autumn of 1920 did these symptoms become more marked; he felt anxiety, palpitation, dizziness, and was easily frightened. In 1920 he was admitted for some time to the Military Hospital in Copenhagen; at times he was delirious, he lived through the scenes of the torpedoing in his hallucinations, and, in addition, there was choreiform muscular restlessness while occasionally he complained of diplopia. He was discharged from military service on account of "traumatic neurosis".

¹⁾ Briand, Staehelin (auto-imitation of diplopia and spasms of cervical muscles, both symptoms disappearing in hypnosis).

Early in 1921 he developed some speech defect, stuttering, "he could not utter the words properly"; simultaneously his gait and carriage became Parkinsonian; there was fibrillation of lips, tongue and hands; he grew apathetic, remained much in bed, became slow in manners and thought, "slow of perception", would repeat several times what was said to him, was somewhat silly; developed a tendency to get into petty debts.



Fig. 37.

Examination in our department showed a somewhat stiffened, immobile, now open-mouthed surprised, now fatuously grinning face, with indistinct lines, some salivation, especially at night. His body and arms showed slight Parkinsonian attitudes (Fig. 37), there was slight bradykinesia and rigidity in the arms, fine tremor in the hands at rest, at a later stage oscillation in the arms in voluntary movements; light bradyphasia; fairly marked bradyphrenia; no emotional-erethic crises. Pupillary reactions, eye movements, eye grounds, tendon reflexes, cutaneous reflexes, humoral syndrome, all normal.

On the whole it not infrequently happens that patients with chronic epidemic encephalitis for a time pass under the diagnosis of hysteria. The incipient parkinsonism, the cerebral or spinal pareses, or the paroxysms (lethargy, coma, etc.), and more especially the hyperkineses, with their often very bizarre muscular unrest, may quite well explain such errors of diagnosis, at any rate in the initial stages of the disease, and if the examination be not very thorough¹).

Thanks to Babinski's fundamental researches, among other things, we are now rather reserved in making the diagnosis of "hysteria" in cases of uncertain etiology, or where the clinical pictures present strange and unknown symptoms. The diagnosis hysteria has almost become our diagnostic "ultimum refugiens". All the more so as we have lately gained a more thorough knowledge of the frequently very intricate and grotesque symptomatology of the extrapyramidal nervous affections.

It is to be regretted that these clinical pictures just fail to show those symptoms from the pyramidal tracts which in other cases afford a reliable aid in the differential diagnosis between hysteria and organic nervous disease. Thus, as far as the extrapyramidal syndromes are concerned, including the encephalitic ones, we must have recourse to a minute analysis of the specific character of the motor disturbances. In the case of the hyperkineses, special stress should be laid on rhythm and localisation — on the mode of onset and further development of the symptoms, and also a very careful search should be made for the presence of other truly organic nerve symptoms. And, finally, a comprehensive consideration and evaluation of the entire clinical aspect of the case, its chronicity, massiveness, progressiveness, will usually lead us to the correct diagnosis, as, for example, the following case reports will illustrate.

¹) Mlle Lévy's statement that, at the demonstration of patients suffering from "bradykinesia" in Soc. de Neurologie at Paris, several of the audience supposed the cases to be hysteria, is of some interest.

Case 53. A married woman, aged 36, admitted 6th January 1923. After a vague encephalitic stage in 1919, she experienced weariness, depression, emotional over-excitability, fits of weeping; she was easily scared, and slept badly. In addition to this general mental impairment she revealed more episodic symptoms such as more persistent pains in the muscles, of from 3 to 4 hours' duration, setting in when she was at rest, but ceasing when she was at her work, when she walked, or the like; and paresthesiæ in the fingers so that she could not hold her needle for sewing. Sometimes, slight jerks would occur, for instance in the abdominal muscles, resembling starting of fright. Or, again, attacks of coarse trembling of the hands. Peculiar to her case were, moreover, fainting fits, associated with a rise in temperature, on a single occasion as high as 40° . Objective neurological examination showed nothing especially abnormal beyond rare myoclonic jerks in the abdominal muscles and occasionally some more persistent muscular fibrillation in different muscles of the legs; there was no parkinsonism, no anomalies of reflexes or pupillary reactions, or the like. Lungs, heart, and urine were normal. Blood pressure 110 mm. No dyscrinic disturbances. The temperature was normal during her stay in the ward. Spinal puncture: cells 12/3, globulins 0, albumins 13. Wassermann reactions negative. She was a dysregulator.

Case 54. A woman of twenty-six, some three years after a mild attack of "Spanish disease", developed neurastheniform symptoms: fatigue, psychic and motor inhibition, some depression, headaches, congestions, vertigo, dyssomnia, impaired memory for fresh impressions, palpitations, fits of perspiration, attacks of pains in cardiac and lumbar regions; no gastric symptoms, however, were observed. Episodically, moreover, she suffered from diplopia, impairment of convergence movement, and left-sided facial paresis being also demonstrable at a certain period.

During her stay in my department from May 1923, a paresis of the left arm associated with hypalgesia, set in for some days. Spinal puncture showed: cells 1/3, globulins 0, albumins 7—8. Wassermann test in blood and spinal fluid negative. Test meal and X-raying revealed a pylorus spasm with rather marked retention, but no signs of gastritis or ulcer. There was no amenorrhea or other vegetative disturbances. No parkinsonism or myoclonia. The temperature curve was "flat", but there was no hyperthermia, no tachycardia, and nothing abnormal in the urine.

The following patient, however, presented the most complete clinical picture of "functional" disturbances in a chronic encephalitis.

Case 55. A woman telephonist, aged 31, single. Previously she has always enjoyed good physical health; occasionally she had some (uncomplicated) headache during the first days of her menstruation, which had always hitherto been regular. Psychically there had been nothing remarkable; emotionally she was well-balanced. She had never had convulsions; on a single occasion she had walked in her sleep, this being subsequent to a severe headache.

In January 1922 she was confined to her bed for 3 weeks with "Spanish disease", fever up to $38,6^{\circ}$, very marked somnolence (she declares however that she could hear what happened around her), now and again she darted up and "talked in her sleep"; she had heavy jerks and fits of twistings of the arms and left leg. There were no definite palsies of eye muscles or visual disturbance. She states that she has sometimes had "red and blue dots" beneath her eyes.

Subsequently she became very tired, grew emaciated, (she has gone down from kgs. 57,5 to kgs. 44,5); her hair has grown white in the vertex region, menses have become very irregular, painful, diminished, often lasting only a day or two. She often has attacks of strong sensation of heat followed by perspiration. No polydipsia, but excessive polyuria and pollakuria; she passes her water about 50 times a day (not in the night); she thinks that she voids about 12 to 13 litres in the twenty-four hours. For a time she frequently had violent palpitation followed by "a standstill" of the heart, associated with precordial pain and anxiety. There was also for a time a tendency to polypnea, usually during sleep: she would wake up with a sensation as if she had "run upstairs to the fourth floor". There were never convulsions or enuresis.

Her memory for fresh impressions and her faculty of reproduction have become markedly impaired; she has however a fairly good memory regarding the earlier events of her life. Her comprehension is likewise impaired: she has to read a thing twice over in order "to catch the meaning fully"; she finds it difficult "to concentrate her thoughts". She is usually in low spirits, will often cry, but there are no anangastic symptoms. On March 7th, 1922, her memory suddenly failed her completely while she was walking in the street, near the place where she lived; she had forgotten what direction she should take in order to get home, could not think of her own name or residence, she roamed about the same square for about half an hour, until a police-man took notice of her; she was however unable to tell him her name or address, nor did she remember the number of her own telephone. Her brother's

number she could remember, but not his district; she had the feeling all through "that it was somewhere at the back of her memory", but she could not catch it. The policeman now tried to lead her down different streets, and at last, on seeing a tree that stood opposite the house where she lived, she knew her whereabouts. She went to bed immediately and slept on heavily all through the night. On awakening next morning she was fully orientated and could remember her fugue. During the fugue her consciousness had not been generally clouded, nor did she feel any real anxiety. She has had no similar attacks later; however, once, in a shop, she could not manage the payment; she saw and knew the coins all right, but could not add them up.

Her sleep was very bad for a time; although she was sometimes so tired that she had to support her lower jaw, which would otherwise drop, she could not go to sleep. During this period she also walked in her sleep a few times: she dreams somewhat, a train is about to run her over, or she is a small child who has got a sixpence from her grandmother to buy cheese at the market, and she quietly leaves her bed, goes into her parents' bedroom and sits down on the floor. However, her sleep has again become good, without heavy dreams.

It is doubtful whether there have been febrile episodes; now and again she has had the feeling as if she had high fever, but when her temperature was taken it never exceeded 37.6°C . in the evening.

During the last three weeks she has been much harassed by pains in the left side of the neck, in left temporal region and left half of face, occasionally also a little pain in the right temple; the pains are stationary, persisting all through the day; in the night she is able to sleep when she wraps her head well up. There is no vomiting or nausea, no disturbance of vision, but strong flushing of the left side of the head and the neck accompanied by a sensation of excessive heat; her left eye waters, the eyeball protrudes, the left pupil becomes appreciably more dilated than the right, and she has a sensation of "numbness" in the left half of the face. There is no swelling of the front cervical region.

During the last fortnight she has a few times fallen down or had a tendency to do so, a sort of vertiginous feeling with forward falling motion though without loss of consciousness, without bruises or involuntary micturition.

She thinks that latterly her speech has become a "little too slow"; neither the patient herself, nor her mother, seem

to have noticed that her movements or gait have become slower or more difficult.

In July 1923 she experienced on one single day no less than three short attacks of diplopia. There were never any other parietic symptoms. Neither has her mother nor the patient herself observed any abnormal involuntary movements, tremor or ataxia.

I had her admitted to my service November 10th, 1923. She is delicate in build, rather slender, weight kgs. 44,200, height ctm 167,5; Sahli (corr.) 105. Many grey and white hairs on the head; abundant pubes and axillary hair. No abnormal pigmentation of the skin. No protrusion of eyeballs on either side, the palpebral fissures are equal in width. Eye movements free; no nystagmus. Alternating anisocoria, the left pupil now and again becoming more dilated than the right (both being usually a little above the average in size). Pressure in the region of left superior cervical ganglion causes marked dilatation of the left pupil, while there occurs no dilatation of the right pupil by corresponding pressure on the right side. Both pupils react promptly to light and on accommodation. Ophthalmoscopic examination revealed normal eye grounds. No tenderness of the trigeminal nerve, but hyperesthesia and hyperalgesia in the left trigeminal region. Facial muscles, tongue, speech, mastication, swallowing, all normal. Respiratory type not appreciably changed during her stay in the ward. Hearing was normal; the vestibular tests showed nothing abnormal beyond a tendency to fall backwards, independent of the position of the head.

The upper and lower limbs are normal in respect of tonus, trophic condition of the muscles, strength, co-ordination, synergies, and sensibility. Tendon reflexes moderately brisk, normal cutaneous reflexes, no Babinski reflex. The gait is natural. There is no tremor of any kind, and no myoclonia.

There is no swelling of the thyroid gland, the pulse varies between 60 and 68, rising to 96 by pressure on the eyeball; constantly regular and fairly strong. Blood pressure 120 mm. Stethoscopy of lungs and heart negative. Diuresis, while at the hospital, 620—1300 cc., micturition 4—5 times in the twenty-four hours. In repeated tests of the urine there was neither sugar nor albumin. Temperature rose a few evenings to 37,8°. Spinal puncture showed 2/3 cells, 0 globulins, 8 albumins; Wassermann test negative in the blood and in the cerebrospinal fluid. An injection of 0,5 ctgr of pilocarpine caused a very violent sweating, but without any noticeable differences in the two halves of the face.

Psychically the patient is lively, fairly intelligent, somewhat easily moved and easily frightened, but no more pronounced

emotional explosions. She sleeps calmly. On one occasion she had some diffuse headache, but not of the above-mentioned type. One day she had a fit of vertigo accompanied by tumbling against the wall.

Her condition improved very rapidly under the treatment with argotropine. She left the hospital in perfect health.

In one patient, who was admitted to the department November 11th, 1923, and who is still under my care, the convulsive fits had, in the beginning, a thoroughly "hysterical" aspect.

Case 56. The patient was a boy of 17 years, without any previous illness; indeed, no reliable evidence of encephalitis was to be obtained. About a fortnight before his admittance, his little sister died, and he was very deeply impressed by her death. At her burial, he had his first fit, and in the following days he had in all 4 fits, of about the same type: Sudden onset, he loses consciousness, falls round, becomes a little cyanotic, with very violent tossing and kicking movements of arms and legs, will cry out loudly, etc. No biting of tongue, no involuntary micturition. The fit will last for about half an hour, afterwards he is a little drowsy. He has total amnesia of these attacks.

In this case, one might certainly be justified in diagnosing a hysteria. But, in the ward, he had true epileptic fits, of momentary or minute-long duration, with clonic convulsions all over the body, involuntary micturition and biting of tongue, postictal comatous state, amnesia. And moreover — and this should be especially noticed —, the spinal fluid showed a strongly marked pleocytosis, the number of cells being 260 (mostly small lymphocytes, some large mononuclears), with 0 globulins, 10 albumins, and the Wassermann reaction negative in the spinal fluid and the blood. For about a week, there was a rather strong hyperthermia and tachycardia, the evening temperature rising to 38.9° , the pulse rate to 128, and a fairly pronounced somnolence or, again, a more delirious state. Some few myoclonic jerks and some fine static tremor were sometimes seen in the arms; otherwise, the neurological examination showed nothing abnormal. No ocular symptoms.

His state has improved very considerably, as has also the spinal pleocytosis, repeated punctures showing decreasing number of cells: 43—22—8, with normal figures for globulins and albumins.

It may be that, in this case, we have an "association morbide", i. e. fits of a purely hysterical (psychogenic) nature, preceding the true epileptic seizures of an encephalitic origin. In the light of our experiences of the polymorphous aspect of encephalitic nervous troubles, I should however think it more prudent to admit a common origin for the two types of convulsive seizures in our patient.

Case 57. In another patient, aged 39, male, the asthenic condition was very marked. He had an attack of fever in 1918, had to stay in bed for a week; there was no pronounced somnolence, nor eye symptoms. After that, he could not recover, felt awfully tired, suffered badly from headaches and giddiness. Sometimes the temperature would rise for a few days, attaining 38.4° in the evenings. In 1919 and 1922 there were true febrile relapses of about 4—5 weeks' duration. For long periods he was quite unable to attend to his work. During the last months of 1922 he was treated in a hospital in Copenhagen. He there complained of pains in different parts of the body, the temperature showed a marked tendency to rise above the normal. In the spinal fluid were counted: cells $2/3$, globulins 0, albumins 8, the Bordet-Wassermann test being negative in blood and spinal fluid. The neurological examination revealed only a sluggishness of the upper and middle abdominal reflexes; no other neurological findings.

He gradually got worse, depressed, and now he also noticed trembling of the hands, especially on carrying food to his mouth, etc. There have been no myoclonic or choreatic movements, no general slowness of voluntary movements, no trouble of speech, no eye disturbances, no increase in weight, no polyuria.

He was admitted to my hospital on the 14th November 1923, in a rather tired and depressed condition, but without showing any real psychotic troubles. Blood pressure 135 mm. Hæmoglobin 100 % (Sahli). No signs of hyperthyreoidism. No general muscular rigidity, nor hypertonia, bradykinesia, troubles of gait or of speech. No palsies anywhere. Pupils equal in size, reacting promptly to light and on accommodation. Eye grounds normal.

In the face, during speech and mimic movements, slight myoclonic jerks were noticed in the corrugators and muscles of the mouth. In the left thumb when at rest, there was a fine, vibrating, not quite continuous, rather quick tremor, which

extended to the other fingers when the arm was raised, and which sometimes became a little coarser, too. On occasions, though only in the raised arms, a coarse, arrhythmical shaking or vacillating was noticed, or a fine, quick tremor was seen in the fingers of the right hand, etc. When he was sitting up, a slight vacillating tremor of the head was sometimes present.

The tendon reflexes were normal; on the left side a doubtful Babinski sign; the abdominal reflexes all present and quick. No sensory disturbances; no ataxia.

A slight systolic murmur was found. The pulse was usually slow, the rate being about 52 to 64. The temperature curve normal, except for 37.8° on the evening of his admission. The urine without albumin or sugar. Weight kgs. 85.500 (average height).

It is hardly of any greater value to give differential-diagnostic indications for the individual hysterical symptoms or syndromes. Some points have already been dealt with in what has gone before. And, as for all hysterical (psychogenic) manifestations, it can be said that the consideration of the individual symptom is, in general, only of relative value, and that the diagnosis requires a thorough analysis of the whole psychic condition of the patient, both as it presents itself for the time being, and also, and more especially, as it was prior to the actual manifestations; a careful searching for the psychic pathemata underlying the clinical picture; a minute analysis of the symptoms or syndromes with a view to their being interpretable, psychologically as well as physiologically, on the basis of the psychic trauma, the "conflict", etc.

There is one further point, only, which I want to mention; namely, the diagnostic value of the fact that the symptoms may be influenced by exogenic and, more especially, by psychic factors.

For, as there can be no doubt whatever that psychogenic and hysterical symptoms and syndromes may (to a certain extent) be influenced by psychic impressions or by spontaneous psychic oscillations in the patient; neither can there be any doubt that also organic nervous symptoms, and primarily, perhaps, such as the extra-pyramidal syndromes, whether encephalitic or non-ence-

phalitic, may prove accessible to similar influences, sometimes to a most astonishing extent. All authors agree in pointing out that the patients in question, voluntarily, at request, as the situation requires, if excited, etc., are able to check even the coarsest nervous symptoms, or even to make them disappear completely for a time. Or, in other cases, symptoms such as, for instance, tremor, are evoked only by emotion, etc. This has, however, been mentioned in the previous chapters (compare "kinésie paradoxale" p. 37, respiratory disturbances, p. 69, hyperkinesia, p. 150, etc.)¹⁾. Possibly, in some cases, a functional component may also be present; but, notwithstanding the grotesque and paradoxical character of these symptoms, an exclusively hysterical or psychogenic causation is out of the question²⁾. The symptoms seen in these cases are primarily a manifestation of an organic hyperexcitability which stamps the psychic life of so many of these patients, and the origin of which perhaps becomes understandable, if we bear in mind that the pathological processes are, to a great extent, localised in the basal ganglia, including also the thalamus, whose importance to the mechanisms of emotion is wellknown; compare later, p. 319.

Diffuse organic cerebral affections with predominant psychotic symptoms, more especially dementia præcox and dementia paralytica, will hardly give occasion for erroneous diagnoses, if only the symptoms and their course of development be closely observed and carefully analysed.

The merely external resemblance between parkinsonism and the more catatonic forms of dementia præcox, has been pointed out previously, on p. 37. Quite apart from the neurologic symptoms, which are quite alien to dementia præcox (catatonia), the "muscular stiff-

¹⁾ Compare also my paper on "Progressive infantile torsion spasm".

²⁾ Compare also Babinski & Charpentier: Rev. neur. 1922 p. 1369.

ening" in catatonia ("Spannungs-Irresein") will, in numerous ways, disclose its psychogenic origin, just as will the catalepsy, the stereotyped movements, the true "catatonic attitudes"; a more intimate psychopathological analysis of the consciousness of the patient will, moreover, reveal disturbances which are entirely different from those found in the bradyphrenic states in parkinsonism (Kirby & Davis, Naville, Stern, Jacob, etc.). The patient mentioned on p. 51 had himself a painful feeling of having "come to a dead stop" in his psychomotor functions: If he wanted to walk, he "had to think of it first", it was "an effort to him to move at all", he wanted "a shove to set him going". Compare also later, p. 316.

However scanty our knowledge is, regarding the causes of dementia præcox, and even admitting that this designation does not cover a nosological entity, but applies only to several etiologically different groups of diseases (schizophrenias, as Bleuler has it, in the plural), we have, as yet, not formed the impression that epidemic encephalitis should play any essential rôle in regard to the etiology of dementia præcox. No increase in the number of cases has been observed in our department, at any rate, such as has been the case with parkinsonism. And, again, the psychotic pictures other than bradyphrenia which, according to our experience, belong to chronic encephalitis, are usually essentially different from those found in dementia præcox, bearing a far greater resemblance to degenerative or psychogenic troubles.

It might be conjectured, however, that the encephalitis virus (as well as, perhaps, other infectious germs) did not produce immediate cerebral changes, but that a certain period of latency occurs after the infection has taken place, — similar to that which is seen in general paralysis, — and not until a later stage do the chronic degenerative changes found with steadily increasing frequency in the nervous tissue and the neuroglia of dementia præcox patients, set in. Or, one might venture the supposition that the encephalitis virus exerts its action

through certain primarily affected, endocrine glands¹⁾. These are, however, until further information has been gained, only loose hypotheses.

As for dementia paralytica, the general psychic picture, the neurological symptoms (speech troubles, hand-writing, etc.) and the practically constantly positive humoral syndrome, afford the clues to a correct diagnosis.

¹⁾ W. Mott has quite recently once more insisted on the relation between dementia præcox and changes in the sexual glands (L'Encéphale 1923, p. 73).

THE HUMORAL SYNDROME IN CHRONIC EPIDEMIC ENCEPHALITIS

In all my patients but two (Case 42 and the patient mentioned p. 187) the Wassermann reaction proved negative in the serum and cerebrospinal fluid.

Some few authors (Achard & Leblanc, Mlle Lévy, and others) state that they have found a weak positive reaction in the serum, though not in the spinal fluid; nor did Guillain find any reaction here. Eskuchen constantly found a negative reaction in both serum and cerebrospinal fluid in cases which did not afford the possibility of a previous syphilitic infection. Stern, too, only once observed a "doubtful" reaction in the spinal fluid. I think we may safely say, then, that the Wassermann test practically always gives a negative reaction in serum and cerebrospinal fluid in chronic encephalitis, a fact which is of conclusive value for the differential diagnosis between encephalitis and syphilitic nervous affections.

Unfortunately, the other findings in the cerebrospinal fluid, viz. the figures for cells, globulins, and albumins, cannot be said to afford any definite diagnostic clue in chronic encephalitis. The pleocytosis and hyperalbuminosis not infrequently found in acute epidemic encephalitis (at any rate in certain epidemics; Stern) and which, therefore, are of no little diagnostic value¹), are either not found at all, or, at any rate, less frequently and less pronounced in chronic cases. In these, the "irregularity" (Stern) is, to a certain extent, a characteristic feature of the findings in the spinal fluid.

¹) Compare Axel V. Neel: *Bibl. f. Læger*, June—July 1923 (danish).

In by far the majority of cases the cell and albuminoid counts yield quite normal figures (Sicard, Guillain, Rodriguez, and others)¹⁾.

According to the investigations of Barré & Reys, as we have previously mentioned, abnormal changes in the cerebrospinal fluid, if such are found, will be found to have disappeared with the eighth month of the illness. The pleocytosis vanishes most rapidly, Stern sought for it in vain in 21 patients in the second and third months of the illness. Mlle Lévy constantly found normal cell figures in her chronic encephalitic cases. Nor does Eskuchen give more than 2 cases with pleocytosis among 16 chronic, "subsided", cases²⁾.

Increase in the globulin contents, usually slight only, was found by Eskuchen in 12 out of 16 cases, by Stern „sometimes“, and not later than the 6th month of illness. Mlle Lévy, Sicard, Guillain, Rodriguez, never found hyperglobulinosis. A hyperalbuminosis, an increase in the nitric acid fraction, was found now and again by Mlle Lévy; Stern and Eskuchen do not mention this point.

Bénard describes a "dissociation cyto-albuminique", namely increased cell-figures, but low protein contents, which also we have noticed in some patients. The diagnostic value of this phenomenon is, however, a little dubious.

As will be seen from our case reports, the findings in the cerebro-spinal fluid also varied very considerably in our patients.

In order to judge whether the findings are normal or pathological, and to be able to compare our results with those of other writers, it will however be necessary to examine what figures should be reckoned as normal for cells and proteins in the cerebrospinal fluid.

¹⁾ Revue Neur. 1921, p. 600—605.

²⁾ Perhaps 3, however, as the author does not include a case showing 12 cells, a figure which, as compared with our "normal figures" (see later) absolutely denotes a pathological finding.

There can hardly be any doubt that the figures usually considered normal, for instance, by Nonne, Bisgaard, and others, have been too high. Dr. Axel V. Neel, my Laboratory assistant, has personally, during a number of years, at the Psychiatric Laboratory of the Copenhagen University, carried out the examination of the spinal fluids of about 1750 patients suffering from the most varying neurologic or psychotic affections, or from physical diseases of quite a different kind¹).

According to these investigations the normal cell count in the cerebrospinal fluid (enumerated in Fuchs-Rosenthal's counting-chamber) should be put at 0—1/3 cells per cubic millimeter.

The normal figures for proteins, determined in the Ross-Jones-Bisgaard apparatus²), are globulins 0, and albumins 10.

If, on the basis of these normal figures, I sum up the results of the findings in the cerebrospinal fluid from the cases of chronic encephalitis dealt with in the present work, the following results appear:

In 33 cases the cell count was 0—1/3, in 23 cases between 2/3 and 9/3, in 9 cases between 10/3 and 30/3, in 8 cases it exceeded 30/3 (the highest figures being 250/3, and 260/3).

Thus, in 55 % of our patients the cell count denoted pathological conditions, if judging by Neel's "normal figures".

¹) Axel V. Neel: Studies on the contents of cells and proteins of the normal spinal fluid. Communications to the Medical Society of Copenhagen 1923, p. 52 etc.; will be published in *Arch. suisses de neur. & psych.*; Dujardin: *Le liquide céphalo-rachidien dans la syphilis*. Bruxelles-Paris 1921.

²) As for this technique of examination and the significance of the figures in question (titre values), cf. Wimmer: *Psychiatric-neurological examination methods*. St. Louis 1919, p. 168—170 (The figures stated as normal in this work should thus be corrected).

Most frequently, however, the pleocytosis was only moderate; and, it was a question almost exclusively of lymphocytosis.

The globulin figures were increased in 6 out of 73 patients, only; the titre value never exceeding 2. Hyperglobulinosis may, therefore, be said to be of rare occurrence or, if found, at any rate, but slightly pronounced in chronic encephalitis, a fact which is of extreme diagnostic value in differentiating it from syphilitic nervous affections.

In 53 cases the nitric acid fraction was below or about the normal titre value (10), in 17 cases it was between 10 and 20, and in 3 cases only, above 20 (highest figure 30).

It is thus relatively more frequently that we find a hyperalbuminosis than an increase in globulins in chronic epidemic encephalitis, the former being found in 27 % of the cases; however, also here the increase is in the majority of cases usually moderate.

In regard to these pathological findings in the cerebrospinal fluid, it was the rule that only one or two, rarely all three figures (Cases 1, 61) denoted abnormal values.

The fact that our cases thus present a somewhat greater percentage of pathological findings in the spinal fluid than those of earlier investigators must, as has been said, be ascribed to our basing our judgment on other "normal values" than the usual ones. The proof of the correctness of these normal figures may be sought for in the above-named paper by Dr. Neel.

According to the foregoing statements we feel justified in attaching a certain diagnostic value to the findings in the spinal fluid of chronic encephalitic cases: In the first place, the pleocytosis will, in the cases where it is fairly pronounced, at any rate strengthen our supposition as to an organic and, on the whole, also an infectious nervous disease, a diagnostic indication which is of no little value, for instance when we are confronted with clinic pictures of a predominantly "neurastheniform" or "hysteriform" aspect.

Moreover, the "dissociation" between the pleocytosis (may be hyperalbuminosis) and the negative Wassermann reaction (in the serum and cerebrospinal fluid) is of considerable diagnostic value in cases where syphilitic nervous affections might come into consideration.

The spinal fluid pressure has not been examined in our patients, at any rate not systematically; in this respect we are inclined to agree with Stern, in not deeming it advisable to attach any special diagnostic value to an increase of pressure, even if such be found. According to numerous investigations undertaken in our department by my former assistant physician, Dr. Schröder, this phenomenon seems to be too capricious in its occurrence to be of any diagnostic value.

Several investigators (Marie & Mestrezat; Netter, Block Dekenver; Dopter; Foster; Stevenson; Sicard, and others) have found increased quantities of sugar in the spinal fluid, a hyperglycorrhagia. Mlle Lévy found it in 14 patients, and Eskuchen, too, ascribes a certain diagnostic value to this symptom. According to Thalhimer & Updegraff¹⁾, the increased percentage of sugar in the spinal fluid may be used for differentiating the acute forms of encephalitis from tuberculous meningitis (and acute anterior poliomyelitis). Mestrezat found a hyperglycorrhagia in numerous nervous affections, chronic or subchronic, such as syringomyelia, amyotrophic lateral sclerosis, tumors of the brain, as well as in a number of syphilitic diseases. Thus, the value of the symptom as to its use for the differential diagnosis, tends to be considerably lessened. Moreover, my former assistant physician, Dr. Kn. Winther, and Dr. Munch-Petersen, have sought for hyperglycorrhagia in 8 patients with chronic encephalitis of a duration surpassing at least one year²⁾. The method used was that of Dr. Hagedorn, of Copenhagen. The results were quite negative, the sugar percentage in the spinal fluid not exceeding 0,041 to 0,067 %, which may be

¹⁾ Archives of Neur. and Psych. 1922 vol. 8 p. 15.

²⁾ Communication at the meeting of the Neurological Society of Copenhagen, November 28th, 1923.

regarded as normal figures. In the blood also, the sugar values were found to be normal (0,08 to 0,094 per cent).

Theoretically, an increase of the sugar contents in the blood and in the spinal fluid should be very interesting, seeing that it might possibly be due to a lesion of the central sympathetic centres in the basal (hypothalamic) regions of the brain (compare below p. 312).

Guillain & Lechelle¹⁾ found their "réaction de ben-zoin colloïdal" negative in a case of chronic encephalitis, a fact, which may occasionally be of importance as a diagnostic factor when differentiating between chronic encephalitis and syphilitic cerebrospinal affections, in which latter the reaction is usually decidedly positive.

The occurrence of a xanthochromia in the spinal fluid or, even, a true spinal hemorrhage, as seen in our case 65, is quite exceptional. Mostly, the spinal fluid is quite clear.

¹⁾ Revue neur. 1921 p. 80.

INOCULATION EXPERIMENTS ON RABBITS.

Through the kind collaboration of Dr. Vilh. Jensen, lecturer on bacteriology at the University Institute of General Pathology of Copenhagen, a number of inoculation experiments on rabbits have been carried out, the animals being inoculated intracerebrally with spinal fluid (or blood) from some of our cases of chronic encephalitis (Cases 28, 36, 46)¹).

Of the total of 71 rabbits inoculated, 7 died from intercurrent illness, no morbid changes being found in their brains; 25 animals were killed with chloroform, while 39 survive.

Subsequent to the inoculation some few animals suffered from epileptiform attacks, but soon recovered, showing later on no nervous troubles.

Of the rabbits killed, 5 were examined less than 100 days after the inoculation; in none of these animals were morbid brain changes found on thorough microscopical examination. From all these animals, re-inoculations on a new series of rabbits, with emulsion from the pons, were made.

4 rabbits (Nos. 1—4) were inoculated with spinal fluid from our Case 28. In none of these animals, on being killed 2, 72, and 437 days, respectively, after inoculation, were any morbid brain changes found, whereas such were found in a rabbit No. 15, inoculated from rabbit No. 2 and, furthermore, in a rabbit No. 27, that had been inoculated with material from rabbit No. 15, these two animals being killed 160 and 230 days, respectively, after the inoculation.

With spinal fluid from our Case 36, rabbits No. 5—7 were inoculated: in No. 5 and 6, on being killed 69 and 210 days, respectively, after the operation, no brain changes were found,

¹) Pette, too, has carried out inoculation experiments on rabbits, with materials from 8 patients, but without positive results.

whilst such were most marked in rabbit No. 7, killed after 425 days. Re-inoculation from rabbit No. 5 in another rabbit (No. 10) produced slight encephalitic changes, the animal having been killed 387 days after the inoculation.

5 rabbits, Nos. 8 to 12, were given an intracerebral inoculation with spinal fluid or blood from our Case 46. On being killed 67, 430, 423, and 452 days, respectively, after the inoculation, rabbits No. 9 and 10 showed, at the autopsy, meningitic changes, whereas in the brains of rabbits No. 11 and 12 true encephalitic lesions were quite evident. A re-inoculation with brain material from rabbit No. 10 produced no encephalitis in another animal, killed after 387 days.

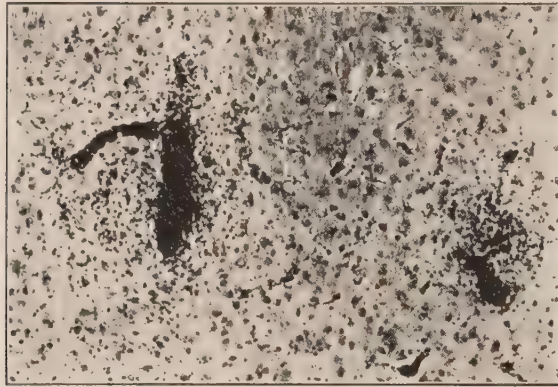


Fig. 38.

Thus, in rabbits, the inoculation period is rather protracted, no morbid brain changes being found until 100 days after the inoculation. Then, again, the primary inoculation may give no positive results, whereas a re-inoculation with brain material from rabbits, which have not, themselves, shown any morbid brain lesions, may give most marked histological changes. As a rule, the probability of finding encephalitic changes in the rabbits increases with the time elapsed since the inoculation. This fact goes very well with the statements of Kling, Davide & Lilienquist, viz. that the incubation period of the encephalitis virus is usually strikingly protracted in rabbits. At least this seems to hold true as regards inoculations from chronic cases such as ours.

In our rabbits, the histopathological picture much resembled the picture described by Kling and his co-workers. Perivascularitic changes, i. e. small mononuclear lymphocytes in the perivascular spaces, were seen in the brains of rabbits Nos. 7, 11, 12, 15 (Fig. 38). The lesions were scattered all over the brain, presenting no predilection, for instance, for the basal ganglia. In addition to these lesions, resembling those of an acute encephalitis, peculiar foci were found, consisting of nec-

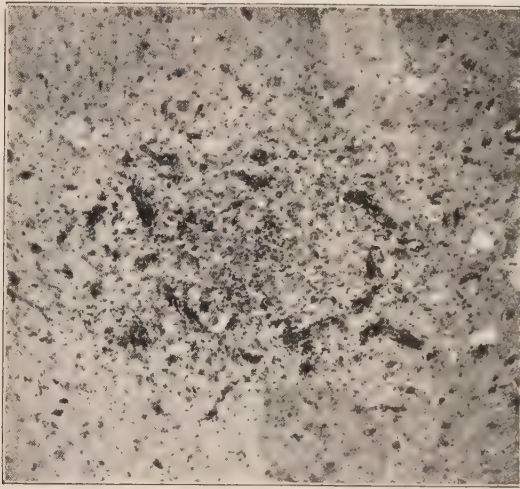


Fig. 39.

rotic centres, surrounded, firstly, by large epithelial cells and then by a layer of small mononuclear lymphocytes. Close to these foci blood vessels with perivascular infiltrations are frequently seen (Fig. 39).

Quite recently, James E. Mc. Cartney, of the Rockefeller Institute, has published the results of a most exhaustive examination of "brain lesions in domestic rabbits"¹⁾. Lesions of a meningo-encephalitic type were found in 55 per cent out of 372 rabbits comprising the laboratory stock regarded as healthy, others with snuffles or dying from different affections, and still others which

¹⁾ The Journ. of experimental Med, 1924, vol. 31 p. 51. 16

were employed for tumor transplantation experiments and treponema pallidum inoculation. The lesions found in these animals were quite like those described above, as clearly seen by the photos given by the author.

These lesions being found in seemingly healthy rabbits, Mc. Cartney criticizes the scientific value of the experiments on rabbits with encephalitis virus, carried out for instance, by Loewe & Strauss, Thalhimer, Kling, and his co-workers. Doubtless, the occurrence of a "spontaneous" encephalitis in rabbits ought to be considered most seriously when we are going to state the nature of the pathologic brain changes found in rabbits which have been inoculated with encephalitic materials. I do not attach too much importance to the similarity as regards histopathologic changes, seeing that the true encephalitic lesions do not present any absolute specificity of histopathology. In Mc. Cartney's investigations, the frequency of incidence of brain changes is most striking. Indeed, one would think that other investigators, too, might have been struck by this frequent occurrence of a "spontaneous" encephalitis in rabbits, if real. Surely, its possible occurrence has been mentioned by a few authors. But I am very disinclined to admit that experienced investigators, such as Levaditi, Doer, and Kling, for instance, should have been deceived by mere spontaneous and accidental brain changes in the animals on which they have performed their numerous experiments. Thus, before rejecting the experimental results of these investigators, I would venture the supposition that the seemingly "healthy" rabbits of Mc. Cartney's have caught an infection of some kind or other, may be an "encephalitic" one. Doubtless, the brain of the rabbit is most susceptible to infectious lesions. And most certainly, the excellent investigations of Mc. Cartney have the great merit of once more drawing our attention to the need of considerable caution when judging the nature of cerebral changes in rabbits experimented on, for instance by inoculation with materials from cases of epidemic encephalitis of man.

PATHOLOGY.

From the preceding chapters it appears with sufficient clearness that in many cases we are unfortunately still groping in uncertainty in regard to the diagnosis of chronic epidemic encephalitis.

In this, as well as in other diseases, the pathology of which is still in course of formation, we have to divide our attention equally between a minute analysis of the symptoms and a synthesis of the clinical features of the disease.

And, in regard to these variable and polymorphous nervous affections which present pictures that are still "new" to us, we will as time goes on learn by our own experiences as well as by those of others.

Valuable, conclusive and instructive information may be derived from a comparison between the purely clinical cases which have come under our observation, and the clinical pictures presented by fatal cases in which the pathological substratum of the disease has been established by an autopsy.

Nine cases with post-mortem findings will be reported in the following pages. These cases should not only provide a small contribution to the study of the pathology of chronic encephalitis; but they are meant also, by their symptomatology and general clinical pictures, retrospectively and by way of analogy to throw some light on the previously recorded purely clinical pictures of the disease, thus supporting, or rendering probable, the diagnoses which have been made.

Medical literature does not as yet contain a very great number of cases of chronic encephalitis that have been evidenced by postmortem examinations (v. Eco-

nomo). Meggendorfer, Trétiakoff & Radovici, Francais & Lhermitte, Foix, Marinesco, Schaller & Oliver, K. Goldstein, Jakob, König, Stern, Mlle Lévy, Claude & Schaeffer, G. B. Hassin & D. B. Rohman, J. Ch. Mc. Kinley, H. Marcus, Urechia, Mc Alpine, and others). The findings of these investigators will be further mentioned later, for comparison with our own personal results.

Case 58. Male, aged 20, single, a joiner; admitted to my department January 19th, 1923, died the 24th of the same month.

"Spanish disease" in 1919 (simultaneously with other members of the family); fever up to 40°C for about 10 days; the patient was extremely weak, though not particularly somnolent; there were no delirium, convulsions, involuntary movements or definite eye symptoms. Since then he became less robust in health, developing a tendency to coughing and perspiration in the night; no insomnia or psychic disturbances, no myoclonic symptoms

He was taken ill again January 12th, 1923, with pains around the right ear, and in the forehead, extending also downwards in the right cervical region, right shoulder and arm. Gradually he became much troubled by these pains; from the fifth day of the illness he became increasingly somnolent, somewhat delirious, would get out of his bed, while simultaneously myoclonic twitches would set in (cf. below) in the right cervical region and right arm; nothing abnormal observed in the right leg or in the left limbs, nor in the face. No squinting.

He was first admitted to the Blegdamshospital (for epidemic diseases), but two days later removed to my department. At the Blegdamshospital his temperature had been between 38 and 39°C . He was restless, delirious, and suffered from severe myoclonic jerking.

On admission to my department and continuing until his death he remained in a typically lethargic state; only on a few occasions did he give a sensible answer when aroused, being otherwise confused and "far away".

A few times he had bleeding of the nose; no vomiting. As for the temperature see curve (Fig. 40).

Right pupil twice as wide as the left one, both reacting to light. No definite ocular palsies. Eye grounds normal. No definite pareses of face or tongue. Speech somewhat staccato, not truly dysarthric. No outflow from the ears, no difficulty of swallowing.

He lay in bed with the trunk slightly curved across the right flank, the head turned halfway towards the right and the chin almost touching the right shoulder, which was elevated and carried forward, while the elbow joint was about half flexed (Fig. 41). The head and the shoulder were moved, almost synchronously, by severe myoclonic jerks, about 40 per minute, fairly rhythmical and equal in amplitude, while occasionally, a more and a less severe jerk would follow, one after another, after which a brief interval would ensue. The myoclonia involved

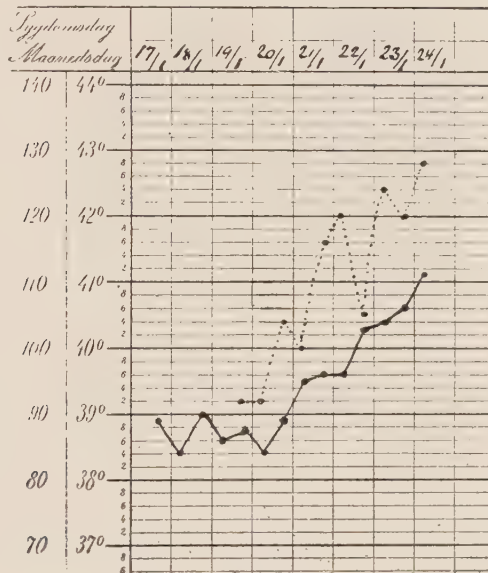


Fig. 40.

the right biceps and, partially, the right brachioradialis, while in the fingers there were only occasionally small extension darts. The muscles named and the right pectoralis were persistently hypertonic. Now and again myoclonic jerking in the left platysma, trapezius, pectoralis and biceps; the latter two muscles were slightly hypertonic. If the head was forced towards the left, severe myoclonic jerks would occur in the right sternocleid. Occasionally the entire right arm would be carried half-way outwards from the body in fluttering movements.

There were no myoclonic twitches in the face; on one single occasion there was some tonic drawing up of the right angle of the mouth.

The rigidity in the right arm was somewhat varying; for a short period there was slight flexion rigidity of right hand and fingers. It also happened now and again that the head could be more easily moved towards the left.

Sometimes there was a fine fibrillation in the muscles of the forearm; coarse trembling of the right arm on attempts at movement.

No myoclonic restlessness or hypertonia in abdominal or leg muscles. No true pareses. Tendon reflexes diminished both



Fig. 41.

in arms and legs. No Babinski reflex. No disturbances of sensibility. Sphincters intact.

Respiration most frequently tachypneic, though on a few occasions there were indications of the Cheyne-Stoke type. Pulse 92—128, gradually becoming soft and slightly irregular. The urine contained 2 % albumin, at a later stage only 1%.

The spinal fluid (somewhat sanguinolent) showed: cells 18/3 (— about 3000 red blood corpuscles), globulins 0, albumins 8; Wassermann reaction in spinal fluid and serum negative.

There was a considerable but transient clearing up of the sensorium. He died during a state of marked somnolence, cyanosis, and irregular pulse rate.

Postmortem examination. Permission was granted to examine the brain only. The dura mater and the soft membranes as well as the visible cerebral vessels were normal. No oedema of the pia. The macroscopic appearance of the brain, on the surface as well as in gross sections, was, on the whole, quite normal; at the most there was some congestion of the cortex and the major ganglia; it is to be noted that there were no definite atrophies, softenings, or hemorrhages.

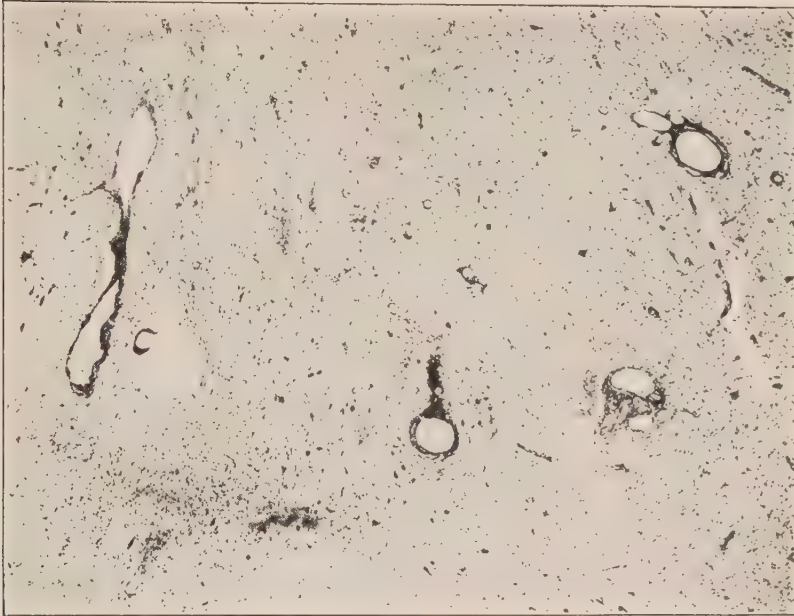


Fig. 42.

Microscopical findings were as follows: In the cortex cerebri there were some very prominent and excessively filled vessels, and here and there some perivascular cellular infiltrations (lymphocytes and some few plasma cells); the walls of the vessels showed here and there a slight hyaline degeneration. The pia had some few foci of lymphocytic infiltration. The architecture of the cells was well preserved, the ganglion cells showing no definite pathological changes. The number of glia nuclei was somewhat increased.

In the thalamus pronounced changes were observed: severe perivascular infiltrations (Fig. 42), made up partly of lymph-

ocytes and plasma cells, partly of the latter exclusively, the vascular walls were beautifully "upholstered" just as in paralytic blood vessels. There were no endarteritic changes, no calcification of the walls of the vessels. In scattered areas of the thalamus there were, moreover, miliary foci of degeneration: pronounced acute and chronic disintegration of ganglion cells, considerable proliferation of the neuroglia with increase of neuroglial fibres; some astrocytes, a few amœboid cells, increase in number of "reposing" glia nuclei, formation of glia rosettes

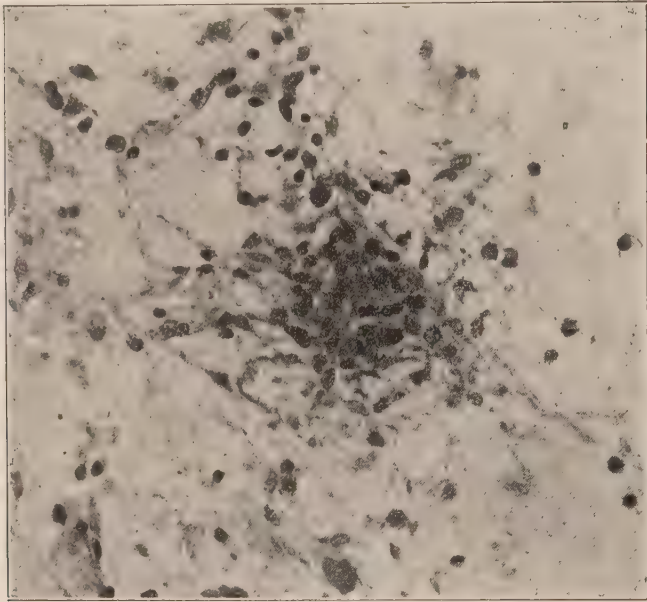


Fig. 43.

(Fig. 42), "glia swarms", but none of Alzheimer's large, "halooned" glia nuclei. Some isolated plasma cells and granular cells were seen scattered here and there in the tissue. The degeneration foci showed no distinct relation to the vessels.

In the corpus striatum the changes were strikingly meagre: a mild degree of perivascularitis, no marked involvement of the nerve cells, no considerable proliferation of the glia.

In the brain stem the changes were, however, more well-marked, below the quadrigeminal bodies, more especially around the aqueduct, the conditions were about the same as in the thalamus, as was also the case in the red nucleus. Also here

the perivascular infiltration was in many places made up exclusively of plasma cells, such cells being also found lying freely in the tissue (together with a few fatty granular cells ("gitter cells")).

In the pons, subependymally, perivascular infiltrations were observed (Fig. 43), likewise in the medulla oblongata, around the aqueduct and also in the area of the pyramidal tracts. The nerve cells seemed to be more or less unaffected. In the cerebrum (also in the dentate nucleus) there were very small

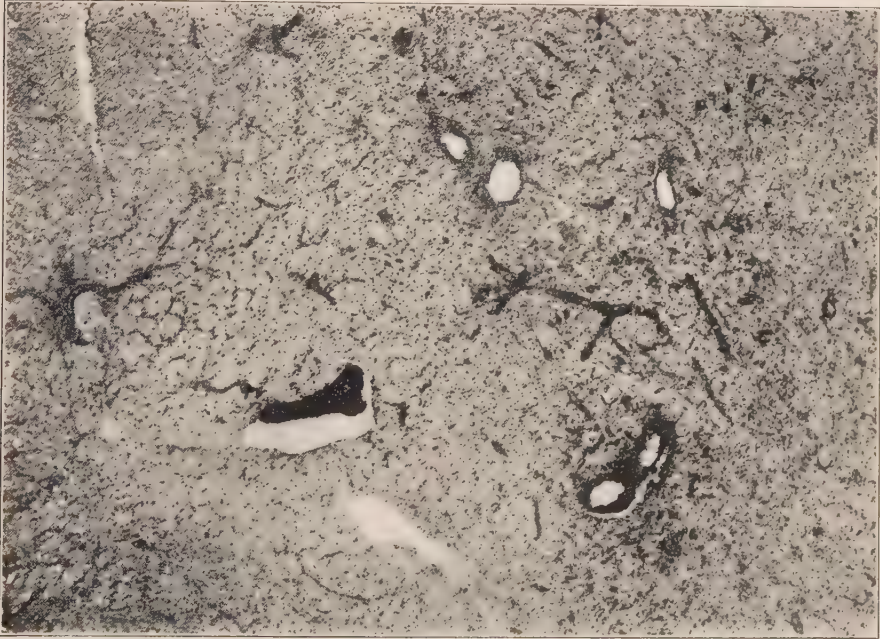


Fig. 44.

lesions, and only a slight trace of perivascularitis. On Weigert hemotoxylin stains, Bielschowsky preparations, with the neuroglia method, no relevant lesions were found.

In this case, neither the clinical nor the pathological picture seem to leave any doubt whatever as to the diagnosis.

What may be discussed here is whether the case was a febrile relapse of a chronic epidemic encephalitis contracted in 1919, or whether it was a reinfection.

In preceding chapters we have occasionally, as for instance on p. 97, made some general remarks as to the possibility of a reinfection in epidemic encephalitis, and in a later chapter this matter will be referred to once more (p. 302). In the case in question here, a reinfection seems less probable than a relapse. Since the encephalitic phase in 1919 the patient had been in a state of a certain debility. And, again, in several other of our reliable cases of chronic epidemic encephalitis the symptoms during the intervals have not been much more marked than in this patient.

The post-mortem findings, as they appear up to the present, seem to me also to a certain extent to indicate a chronic epidemic progressive encephalitis: the diffuse degeneration of the nerve cells, the marked occurrence or predomination of plasma cells in the perivascular infiltrations (notwithstanding the rapid course of the disease), and, finally, the miliary parenchymatous degeneration foci; all findings which in fact correspond very well with those of a chronic epidemic encephalitis, even if, however, they are usually more pronounced than in this case.

Case 59. A country labourer, aged 39, under my care from October 25th to December 15th, 1920. Six months previously he had been laid up with "influenza" for about a fortnight. A few weeks later he noticed tremor in hands and arms, difficulty of speech, he "could not get the words out". During the last few months also difficulty of gait has appeared, he has had no command over his legs, and has fallen down a few times. His memory began to fail him, and gradually he became clouded in mind as well as restless.

When first observed in the ward he was emaciated, in appearance somewhat worn-out. Mask-like face, but no definite facial pareses. No ptosis, no squint or nystagmus; pupils only react sluggishly to light. Eye grounds normal. Vestibular reactions normal; he is somewhat deaf owing to an affection of the middle ear. The tongue deviates toward the left, fibrillates somewhat, amounting to severe jerks on protrusion; synchronously, small twitches in the lips and more especially in the platysma. Speech drawling, slightly scanning, somewhat explosive.

Severe motor restlessness of head, trunk and limbs, of a complex character: partly coarse, choreatic jactitations, partly a more persistent fine tremor, or, again, small myoclonic darts, sometimes involving only isolated segments of muscles. No fibrillation of the facial muscles. Gradually, his movements became incessant, like a nodding doll. Attempts at making him sit up or stand on his legs, provoked a violent static swaying, augmented choreatic jerking, eventually amounting to a true choreatic dancing (with a tendency to retropulsion); when he

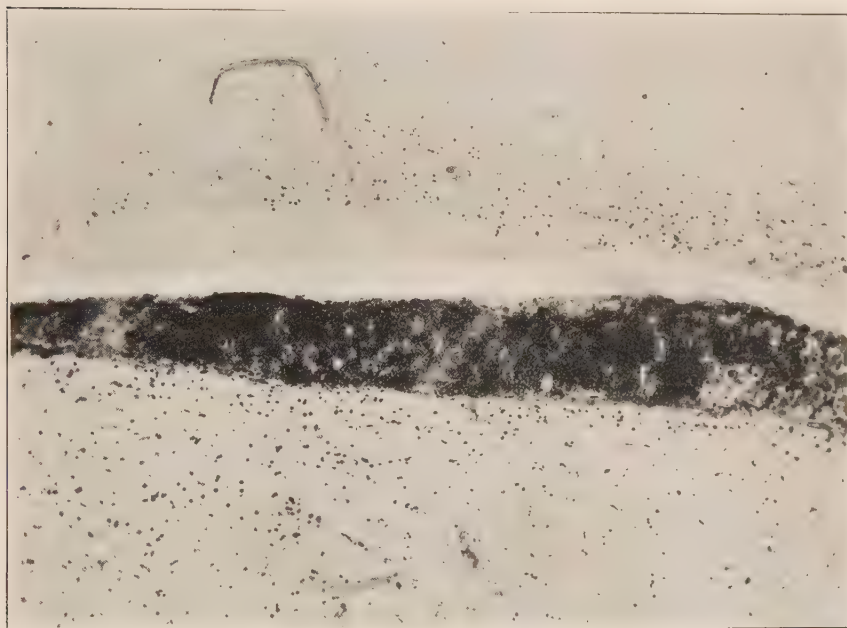


Fig. 45.

tries to walk he tilts backward with choreatic tossing of the legs; if he himself tries to sit on end in his bed, both legs are carried straight upward. In both arms there is marked oscillatory movements when in action.

No pareses of the limbs, no persistent hypertonia, tendon reflexes of average intensity, no clonus, no Babinski reflex. The abdominal reflexes are not present; the cremasteric reflexes preserved. Owing to his mental deterioration it was impossible to examine the sensibility; there was incontinence of urine and fæces.

Spinal puncture showed: cells 1, globulins 1, afbumins 20; Wassermann test in cerebrospinal fluid and blood negative.

Throughout his stay in the ward he was confused, disorientated, hallucinated, had morbid fears, shouted, was very restless and would get out of his bed; his physical debility and emaciation increasing. A rise of temperature occurred coincident with the development of bedsores (previously the temperature had been normal). On December 15th he was removed to St. Hans Hospital; here the speech disturbances



Fig. 46.

and motor restlessness became still further aggravated; he died December 25th, 1920 from a bilateral pneumonia.

The autopsy¹⁾ showed: the left hemisphere was a little smaller than the right. Frontal sections through both hemispheres present well-marked atrophy of the central ganglia on both sides, also of both insulæ Reilii and of both temporal lobes. The

¹⁾ To Dr. C. Berthelsen, Departmental Chief at St. Hans Hospital, who has most kindly placed the preparations at my disposal, I offer my best thanks.

meninges covering the atrophic lobes are very much thickened. There is no softening or hemorrhage, and no macroscopical arteriosclerosis.

Microscopic examination: The central ganglia, both the caudate nucleus and the lens, the thalamus and the sub-thalamic region, were found to be the seat of a pronounced glia proliferation, with numerous large glia cells and numerous glia fibres. The ganglion cells were markedly changed, chiefly atrophied. Specific staining of medullary sheaths revealed no

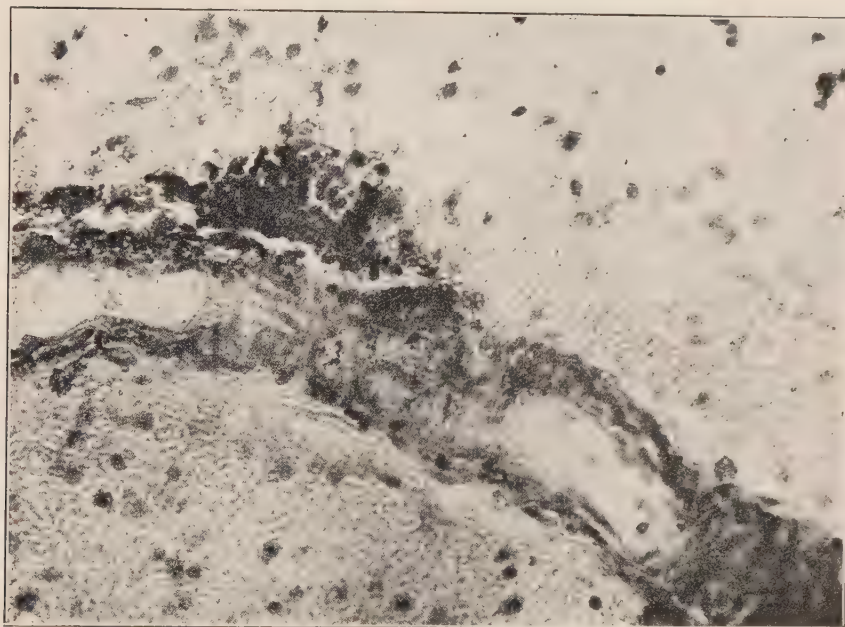


Fig. 47.

coarser degeneration. The vessels showed thickened walls, often with calcareous deposits; in the globus pallidus this state was especially marked (Fig. 45); not only were the walls of the larger vessels found to contain calcareous deposits, but also along the capillaries such could be detected in beadstring arrangement, as well as scattered throughout the tissue; these small concretions were found more especially in the most oral segment of the globus pallidus. In several places small perivascular collections of cells were found, most frequently consisting of

fatty granular cells, but also lymphocytes; no plasma cells. No true softenings could be detected microscopically.

In the atrophied temporal lobes and islands of Reil there was also a marked proliferation of glia tissue, with glia fibres all through the cortex. The meningeal thickening in these areas was chiefly of a fibrous nature, only a few lymphocytes were found.

The remaining portions of the cerebrum presented almost everywhere severe alterations of the ganglion cells and proliferation of glia cells, but without any marked formation of

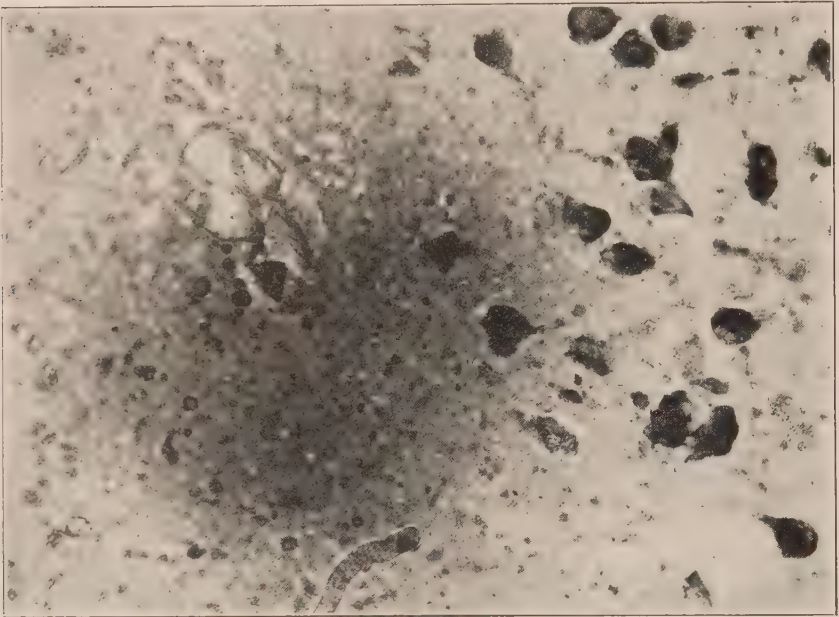


Fig. 48.

glia fibres. The vessels showed a tendency to thickening of the walls everywhere; here and there fatty granular cells and a few lymphocytes were seen in the perivascular spaces. There were no calcareous deposits in the cortex, not even in the areas which were most severely attacked. Nor were there any demonstrable Fischer-Redlich plaques (or Alzheimer's changes of the neurofibrils).

In the medulla oblongata, in its most oral portion, just below the ependyma on the right side, a few thrombosed vessels could be seen even with the naked eye (Fig. 46); also in some

of the other sections these thromboses proved to extend upwards in the ponto-cerebellar tract; microscopically, besides these fresh thromboses, the vessels were seen to be surrounded by lymphocytes (Fig. 47); and the cells of the walls somewhat proliferating. The whole process gave the impression of being of rather recent

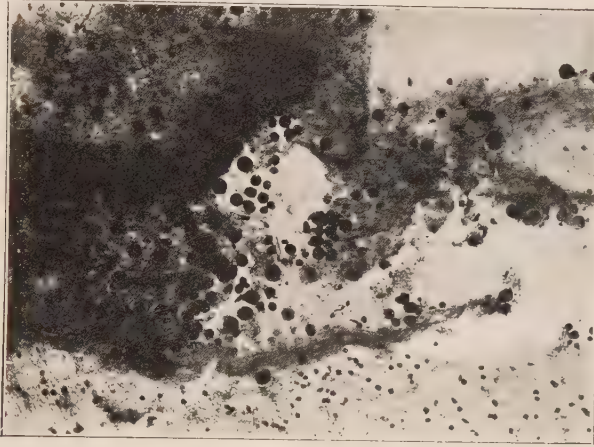


Fig. 49.



Fig. 50.

development. The nerve cells were fairly intact throughout. However, in patches (around vessels?) apparently pure parenchymatous degeneration with destruction of nerve cells was seen, desintegrating glia fibres and small calcareous particles and amyloid bodies scattered all over the tissue. (Fig. 48). In other places, there was a strong proliferation of glia fibres,

amyloid bodies and smaller and larger calcareous particles being visible (Fig. 49).

Farther downward in the spinal cord no coarse lesions were found; myelin sheath staining showed no degeneration of the tracts.

Cerebellum: the cortex presented nothing abnormal. In the dentate nucleus, however, the walls of the vessels were thickened and presented calcareous incrustation here and there (Fig. 50 and 51); surrounding the vessels some fatty granular cells were seen

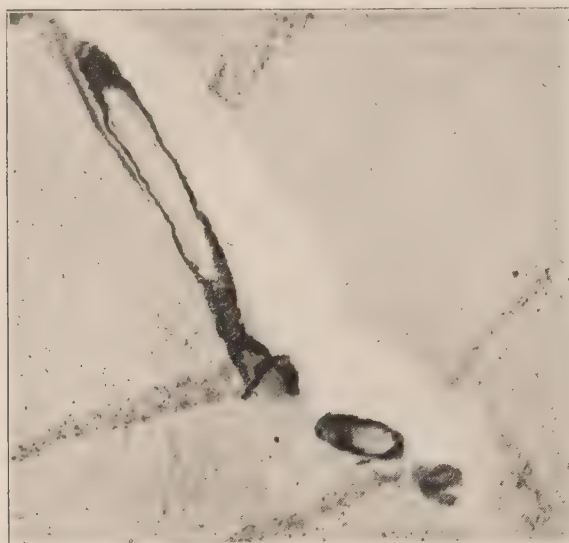


Fig. 51.

In its main features the post-mortem examination thus showed: a localised cerebral atrophy (involving the central ganglia, the temporal lobes, the insulæ Reili); a diffuse degeneration of the nerve cells of the cerebrum with considerable glia proliferation and a peculiar affection of the walls of the vessels and also the appearance of calcareous concretions; all this being more pronounced in the central ganglia and especially in the globus pallidus where the process has evidently existed longest, showing relatively slight inflammatory infiltrat-

ion of the vessels. The perivascularitis appeared to be more marked and of more recent occurrence in the brachium conjunctivum of the cerebellum.

There was thus a blending of more chronic (subsided?) and fresh encephalitic processes. Finally, there were the miliary tissue degenerations which were apparently purely "parenchymatous" (compare below).

Clinically the hyperkinetic-amyostatic syndrome was the predominant feature in this patient; sometimes the case reminded one of a chronic chorea, sometimes of an "atypical" disseminated sclerosis at an advanced stage.

However, the severe psychic disturbances (which might find their explanation in the diffuse involvement of the cortex cerebri) put a stamp on the clinical picture which made it extremely difficult to analyse it. The close chronological continuity with the infectious disease ("influenza") however, made the diagnosis of a chronic or subchronic epidemic encephalitis the most likely one. This diagnosis was corroborated by the autopsy.

The severe involvement of the central ganglia corresponds very well with the marked extrapyramidal syndrome found in this patient. The fresh inflammatory process in the right brachium conjunctivum of the cerebellum and in the caudate nucleus have doubtless a decided relation to the choreatic component of the kinetic disturbances. Again, the speech disorders, which ultimately amounted to an almost unintelligible anarthria, but without definite sensory aphasia, may be purely lenticular, though they may equally well, and with great probability, be partly attributable to the atrophy of the islands of Reil.

The next patient, too, presented an extremely marked hyperkinetic-extrapyramidal syndrome.

Case 60¹⁾. A restaurant-keeper, married, aged 53, admitted to my department April 18th, 1921. He denies syphilis and

¹⁾ This case was reported in the Copenhagen Neurological Society Nov. 30th, 1921.

chronic alcoholism. In November 1918 he had the "Spanish disease", was in bed four days with fever, but no definite nervous symptoms and no marked somnolence. Since that time he has had a tendency to develop bronchitis, has been very susceptible to cold, has suffered increasingly from fatigue, has grown thin and often had headaches, vertigo and vomiting. In February 1921 disturbances of sight set in: "the letters fused together" when he was reading, but there was no real diplopia. Almost simultaneously his head and his arms began to shake; there was, moreover, a noticeable disturbance of speech as well as "difficulty in swallowing" (compare below), so that he was able to take liquid food only. Twice there was retention of urine. No apoplectiform attacks. His state was severely progressive.

On admission he was markedly emaciated; there was no localised muscular atrophy. No bed-sores. Some peripheral arteriosclerosis was palpable. Blood pressure 120 mm. Pulse normal in rate and rhythm. The pulmonary area was enlarged, the lungs covering the heart so as to produce distant dull tones. The hepatic dulness strikingly diminished, that of the spleen indistinct. There was no blood, sugar or albumin in the urine. Normal temperature.

Psychically, the patient was clear, though he did not fully realise his condition. His speech was sometimes thick, drawing, slightly jerky, sometimes peculiarly falsetto and somewhat explosive.

There was some amimia of the face, brows drawn up, an "astonished" expression. Frequent winking movements or small clonic twitches in the orbiculares oculi, especially on the left side; the left eye is frequently for long periods the site of a strong blepharospasm. Spasmodic, grimacing, associated movements of all the facial muscles during speech, by forced opening of the mouth, etc. No definite pareses of face or tongue, no fibrillation of lips or tongue.

The eyes are constantly in a condition amounting to perpetual unrest, partly nystagmoid, lateral, partly a more clonic rolling of the eyeballs in almost all directions. This unrest is aggravated in the lateral positions. The movements of the two eyes are coordinated. The moving of the eyeballs persists under the closed eyelids. In addition, the eyes show a tendency to conjugate deviation towards the left.

The patient lies nearly always with his head and upper body slightly lifted from the bed, the head turned a little towards the left, and a marked contraction of the right sternocleid. There is almost continuous shaking or oscillating of

the head, moderate, irregular, a polymorphous alternation of torticollis spasms and spasmus nutans; occasionally he completely resembles a nodding doll. In the right sternocleid small, clonic jerks frequently occur; also in the deep cervical muscles intermittent clonic unrest is palpable.

Some tremor is now and again seen in the arms at rest, but much more pronounced, however, is a coarse action tremor, a flabby missing of the aim on the finger-to-nose test, and a static oscillation of the limb when the object is at last reached: all this is most marked in the left hand. In the

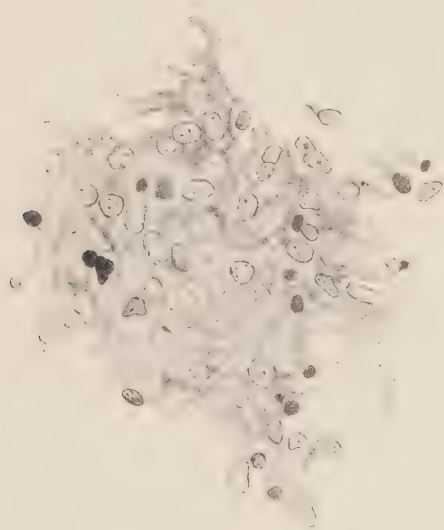


Fig. 52.

elevated arms there is amyostatic oscillation amounting to fluttering movements. With vigorous action of the arms the tremor will spread all over the body in the form of coarse, jerky starts. When he sits erect (which he can only do when supported) there is violent rocking and shaking of head and trunk, like a ship in a heavy sea. In attempting to raise himself on end, both legs will be lifted straight upwards and he will rock on his buttocks. Walking is possible only when he is supported on both sides, and then with somewhat straddling legs and retro-pulsion.

In the dorsal position there is now and again some myoclonic jerking in the adductors of the legs and some coarse action tremor evident both on elevation and on the heel-to-knee test.

The muscular unrest ceases during sleep and subsides considerably when the patient assumes a proper resting position; whilst during all movements and also under psychic influences it tends to increase.

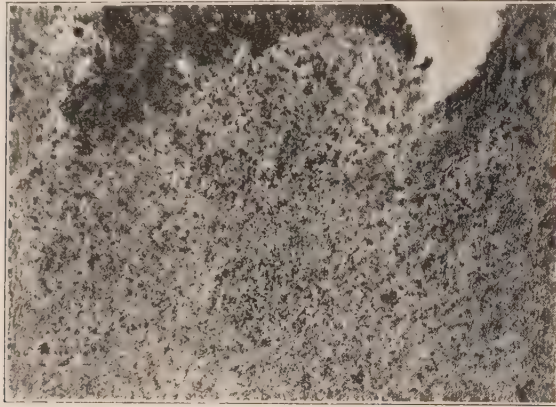


Fig. 53.

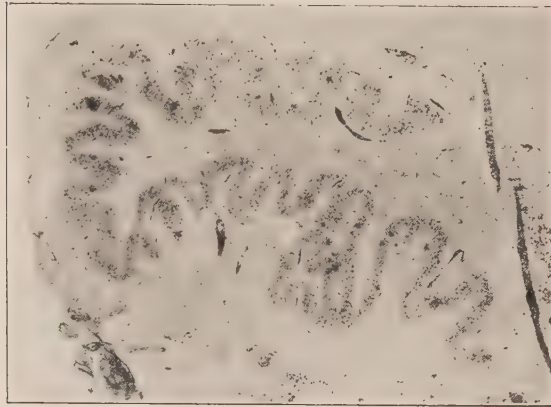


Fig. 54.

There are no definite pareses; the strength of the arms and hands, for instance on shaking hands, seem even to be strikingly good; there is no distinct bradykinesia. No localised muscular atrophy; electric testing showed some diminished excitability to both kinds of currents in the most emaciated groups of muscles, but no degeneration reaction. The mechanical

muscular excitability was markedly increased, to such a degree that, by percussion, the muscles could be brought to project and would thus persist for long, "like ropes with knots"; no myotonic perseverance on voluntary movements. No true fibrillation of the muscles; occasionally, however, some slight myo-cloniform unrest in the abdominal muscles.

There was no definite hypertonia in arms or legs; the tendon reflexes were all brisk, and there was no clonus; plantar reflexes of pure flexor type; abdominal and cremasteric reflexes lively. Sphincters intact. No disorders of sensibility.

No definite abnormal synkineses. Distinct adiadokokinesis on the right side. Testing of vestibular and acoustic functions showed normal conditions.

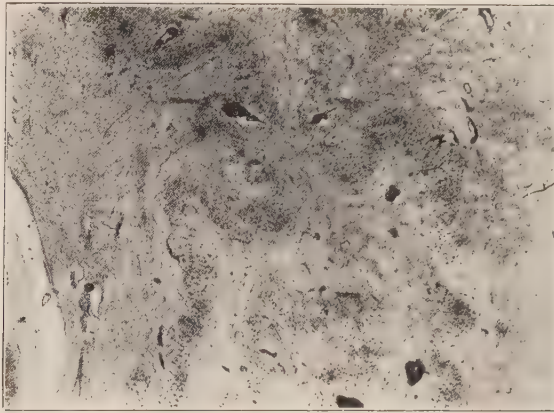


Fig. 55.

No ocular palsies; eye grounds, acuity and fields of vision, pupillary reactions, all normal.

His "difficulty of swallowing" proved to be a dysmasia; he was unable to chew solid food and to turn it in the mouth; finely cut and liquid food he could swallow all right. There was no paresis of the palate.

Towards the end of his stay in the hospital there were vague signs of bronchopneumonia; two attacks of dyspnea accompanied by violent stridor; no arrhythmia cordis was observed here.

Spinal puncture: cells 1/3, globulins 1.5, albumins 30; Wassermann tests in serum and cerebrospinal fluid negative.

His condition grew steadily worse, he became more and more emaciated, had frequently fits of vomiting, bedsores developed, and at last distinct pulmonary symptoms with terminal rise of temperature. Just before death the involuntary movements subsided almost completely. He died August 25th, 1921.

Postmortem examination showed: emphysema, bronchopneumonias, fibrosis myocardii. No definite pathological changes could be detected in the liver, neither macroscopically, nor microscopically.



Fig. 56.

Macroscopically the brain showed no distinct arteriosclerosis, no distinct atrophy of the convolutions, whereas gross frontal sections showed the central ganglia to be somewhat vague in texture and diminished in volume. No hemorrhages or softenings could be detected with the naked eye.

Microscopically the cell architecture of the cerebral cortex was in many places found to be disturbed; there was also a chronic degeneration of the ganglion cells (shrinking, pyknosis, shadow formation), with slight "neuronophagia" in the deeper layers of the ganglion cells. The neuroglia tissue

showed some proliferation with various forms of nuclei, some few astrocytes and amœboid cells, no essential fiber formation, some glia rosettes and glia swarms (Fig. 52). Around the vessels, which show no independent changes, there are here and there slight perivascular infiltrations (lymphocytes, and especi-

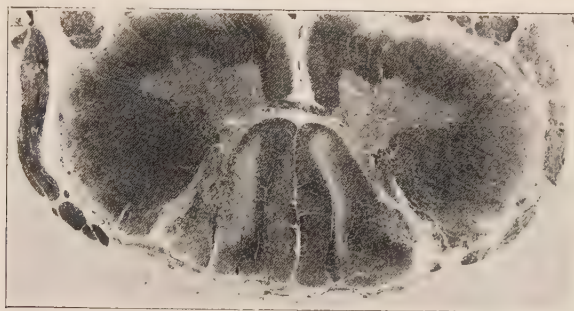


Fig. 57.

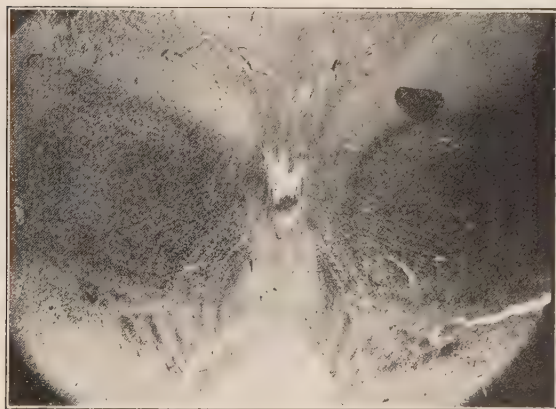


Fig. 58.

ally plasma cells). In many places, surrounding the vessels or spreading more or less out into the tissue, some roundish or oval or pearshaped structureless bodies, larger or smaller in size, are seen; these small bodies assume a faint reddish violet tint when stained with toluidin; there are also some glia cells containing lipoid and fatty granular cells.

In the left thalamus (inner nucleus) there is a fairly large focus with numerous fatty granular cells, marked glia prolifera-

ration, and disappearance of nerve cells (Fig. 53). In addition, in the thalamus as well as in the striatal nucleus, the caudate nuclei, pons, medulla oblongata, the vessels are in many places infiltrated by lymphocytes (Fig. 54). In the dentate nucleus of the cerebellum the perivascular infiltrations were especially pronounced, showing lots of plasma cells (Fig. 55,56); also in the medullary substance of the cerebellum some plasma cells were seen surrounding the vessels, and a well-marked glial reaction.

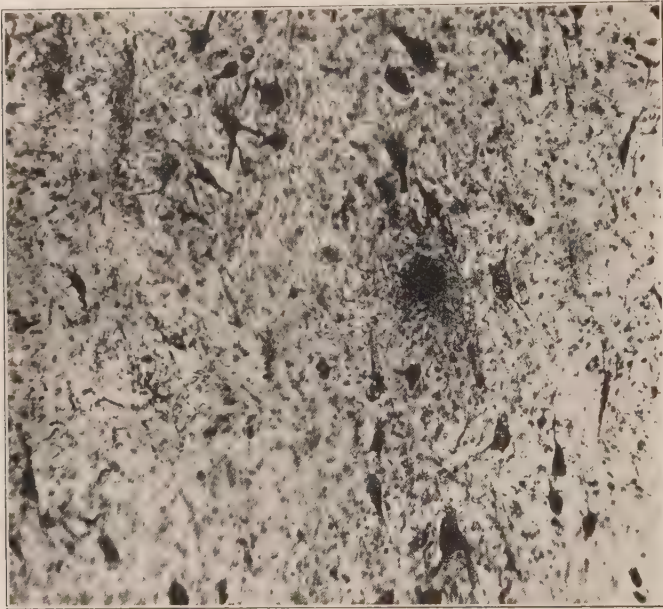


Fig. 59.

Within these segments no more coarse alteration of the ganglion cells was evident.

Staining of the medullary sheaths showed in the pons degeneration of crus cerebelli ad pontem on the right side; in the spinal cord degenerations in the areas of the posterior columns on the two sides (Fig. 57). Staining with Marchi's method showed some degeneration in the nucleus ruber (Fig. 58).

In the spinal cord there were perivascular processes and degeneration of ganglion cells in the anterior horns (Fig. 59); slight perivascular infiltration in the degenerated parts of the posterior columns.

In view of the patient's age an arteriosclerosis would at once suggest itself. However, the peculiar aspect of the clinical picture, as well as its striking similarity to other reliably diagnosed chronic encephalitic cases, and, again, the possibility of connecting the disease chronologically with a preceding attack of "influenza", all these features, as well as others, made us insist upon the diagnosis "chronic epidemic encephalitis", which is also fully confirmed by the post-mortem findings.

Case 61. A young clerk, aged 17, died in my department May 7th, 1922. Not until a few days before his death, through a casual visit of the patient's sister, did I get the anamnestic information which fully corroborated the diagnosis I had previously made by way of supposition.

The patient's father had died in the Rigshospital, in 1919, suffering from a "typical paralysis agitans" (as to the possible infectious origin of which no information could be obtained).

The patient had been apparently dead at birth and had always been rather delicate in health. In his twelfth year he had a slight lesion of the head, without marked sequels.

In April 1918 (when living in a provincial town) he was suddenly taken ill: high fever for about a week, up to 41.7°C , violent pains in the head, marked somnolence, alternating with delirium, vomiting, squinting, diplopia; no ptosis, no difficulty of speech or swallowing, but slight rigidity and reduced mobility of both legs. No definite muscular unrest. A few weeks later he was admitted to the Rigshospital¹⁾, where a slight left-sided hemiparesis was observed in the face, the arm and the leg²⁾; there was ataxia and astereognosis in the left arm, diplopia, dizziness, headache. He seems also to have had convulsions during his stay there. At the neurological out-patients' clinic of the Rigshospital the following diagnosis was made: "pathological process" (tumour?) located in the arm-centre of the left hemisphere, probably behind the Rolandic sulcus. The clinical picture does not seem to indicate a "sclérose en plaques". The patient was given four treatments with X-rays, which, according to the case-book of the clinic, resulted in the disappearance of all the symptoms.

¹⁾ Apparently without the hospital staff getting any information as to the encephalitic phase.

²⁾ The sister thinks she can remember that the hemiparesis set in about a week after the fever had subsided, little by little.

In October of the following year he was, however, readmitted to the Rigshospital; he had a sensation of numbness in the left hand, otherwise no complaints. Objective examination showed: slightly reduced sensibility in the left hand, slight stereoagnosis, coarse shaking of both arms on the finger-to-nose test, sluggish abdominal reflexes, slight universal hyperreflexia; no Babinski reflex, no nystagmus, no speech disturbance or bradyphrenia. One month later a neurological examination revealed: a cortical paresis of the facial muscles on the right side, some wasting of the small muscles of the left hand, distinct Babinski reflex, no definite pareses of the limbs, or disorders of sensibility.

In November 1920, he was once more in the Rigshospital; there was now mild left-sided hemiparesis, bilateral Babinski reflex, and frequently headaches.

November 30th, 1920, he was removed to my department, as he had begun to have convulsive seizures, first in the left arm and leg, and, on the day prior to his removal, generalised convulsions, almost without cessation.

Immediately after his admittance to our department he had an epileptiform, generalised, convulsive seizure, with clonic jerks in the flexed arms and extended legs, frothing, cyanosis; no involuntary micturition, no biting of tongue; the pupils reacting to light. Almost throughout the whole of that day he was in a status epilepticus. On the next day he had a more tetaniform convulsive attack, with purely tonic rigidity, without proper jerking, without loss of consciousness, passing of urine or biting of tongue; the pupillary reactions were also preserved, and there was no Babinski reflex; this attack lasted about half a minute.

Similar tetaniform attacks occurred on the following three days. Objectively, slight paresis of left arm and leg was found (more accentuated after the seizures had passed), slightly hemiparetic gait, brisk tendon reflexes, but no clonus, no Babinski reflex, abdominal reflexes present but weak, slight ataxia of left arm and leg, slight left-sided hemihypesthesia, preserved sense of position and localisation. There were no tongue paresis, and there was no distinct disturbance of speech. Slight divergent squinting of the left eye. The left upward movements of the eyeballs were defective; also impairment of convergence movements was observed. Diplopia, producing pictures which would indicate a paresis of left superior rectus muscle. The right pupil was slightly more dilated than the left; reactions to light and on accommodation well preserved. Slight pallor of the temporal portion of the optic discs, slight temporal defect of the visual field in the left eye.

Spinal puncture: cells 28/3, globulins 0, albumins 10. Wassermann tests in blood and spinal fluid negative.

During the remainder of his stay in the hospital he had numerous convulsive seizures; on one occasion he was 17 hours, on another 12 hours in a status epilepticus: usually he did not quite lose consciousness, but he was often delirious, wailingingly complaining of headache, shouting, tossing about in his bed, often in a marked opisthotonus, or bending forward with flexed arms, or, again, with tetaniform extension rigidity of all limbs, or risus sardonicus. During one of the attacks distinct bilateral Babinski reflex was elicited. On no occasion was there biting of the tongue or involuntary micturition. The duration of the individual fits rarely exceeded half a minute.

He was discharged and removed to his home January 6th, 1921, to be readmitted however June 4th, of the same year; he says that he has been well since his last stay at the hospital, until a few days prior to his readmittance, when he was hit on his head by a heavy book, which resulted in his having a convulsive fit.

His family informed us that, psychically, he had changed strikingly. He had developed mythomaniac tendencies, telling about fires he had extinguished, about people he had saved, boasting of being very well off, being "sole heir to a large fortune", etc. He had become very dull, was quite unable to hold his own at the mercantile school he attended. Occasionally he was very depressed, and he was suspected of having attempted to commit suicide.

In the ward he made a more dull, fatuous impression, somewhat puerile, but not confused. His moods were changing, sometimes he was euphoric, talking nonsense, would boast of all the girls who would have liked to have him for their sweetheart.

Neurological examination gave no new findings. One night, after a violent headache, there was a transitory confused state; the following morning he said that he could remember nothing about it.

He was taken home again on the 26th of June, but readmitted 3rd October 1921, the chief reason being that he had commenced to go "sharking". He went to see a principal of a National High-School and allured him to give him 200 shillings, feigning that he was a "poor orphan"; afterwards he spent all money on chocolate. Psychically his condition was similar to that of his previous stay; he was ashamed and "penitent". During his stay he had no convulsive seizures; there was mild left-sided hemiparesis and doubtful Babinski reflex. On October 21st he was

removed to St. Hans Hospital, where he is said to have had numerous tetaniform attacks. He proved to be an "orthoregulator".

On the 25th February 1922 he was readmitted to our department; psychically he was now very poorly, extremely fatuous, uncleanly, could not help himself in dressing, eating, being unable to grasp anything with his hands.

There was amimia of the face, his expression being blubbering; speech nasally indistinct, though not scanning. The left pupil was more dilated than the right; the pupillary reactions preserved; slight inwards squinting (paresis of the left abducens

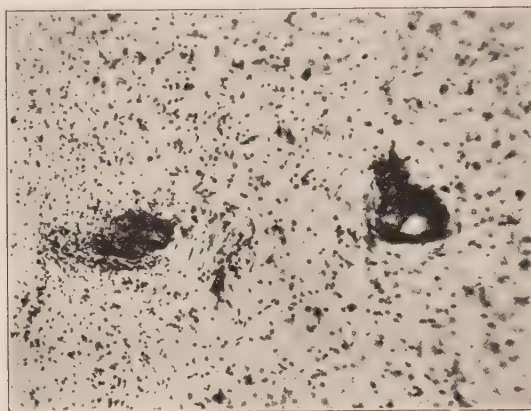


Fig. 60.

muscle). Left-sided hemiparesis just indicated, with a fairly constant Babinski reflex, though no clonus. Eye grounds normal. Spinal puncture: cells 23, globulin 1, albumins 20; the Wassermann reaction was constantly negative in serum and cerebrospinal fluid.

Both physically and psychically there was now increasing debility, vomiting, excessive emaciation. When touched, for instance when the nurse assisted him in dressing, his arms and legs would stiffen in flexion contractures; however, there was no persistent spasticity. In all spontaneous movements of head, arms and legs, there was coarse action tremor. Speech gradually inarticulate, amounting to an unintelligible grunting. The psychic cloudiness was rapidly increasing.

The temperature was normal up to some time before death, when bed-sores developed, and there were irregular rises of

temperature. There was no albumin, sugar or urobiline in the urine. He died May 7th, 1922.

Permission was granted to examine the brain only.

Macroscopically there was slight thickening of the pia mater over the parietal lobes; no hemorrhages or softenings, no marked vascular changes, no distinct atrophies in the gross brain sections.

Microscopically, perivascularitic changes were found in the cortex cerebri (in the frontal and parietal convolutions) in the basal ganglia (Fig. 60); the pons, cerebellum (Fig. 61), and

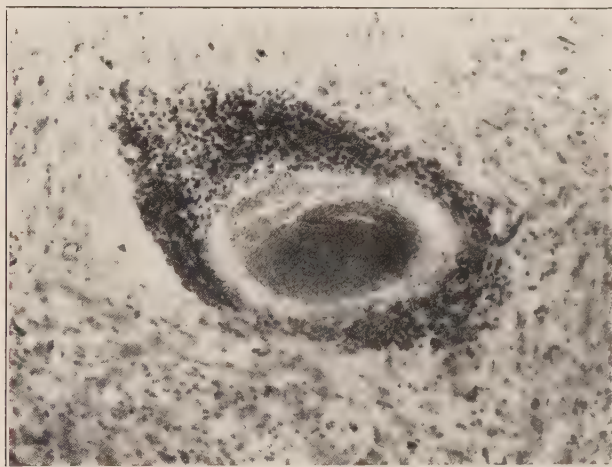


Fig. 61.

medulla oblongata), these changes having partly the form of voluminous accumulations around the vessels of lymphocytes and plasma cells, partly of a more discrete "upholstering" of the walls with plasma cells exclusively (Fig. 62), strongly suggestive of the picture found in cases of general paralysis. In many places the tissue was more diffusely infiltrated with plasma cells. There was also some infiltration of some few vessels in the pia mater (Fig. 63), new-formed connective tissue fibrils, fibroblasts, and in some places disintegration-cells.

The perivascular infiltrations were most numerous and most intense in the basal ganglia, being almost uniformly pronounced in the thalamus and the corpus striatum. In many places the perivascularitic changes were grouped in "foci" with numerous

streaks and interlacing of infiltrated vessels, the cellular infiltrations consisting chiefly of plasma cells, of degenerated ganglion cells, and proliferation of small glia nuclei; there were also some astrocytes; located in a certain area in the right frontal gyrus there was one such focus consisting of numerous fatty granular cells. In the other brain sections such granular cells were only evident here and there.

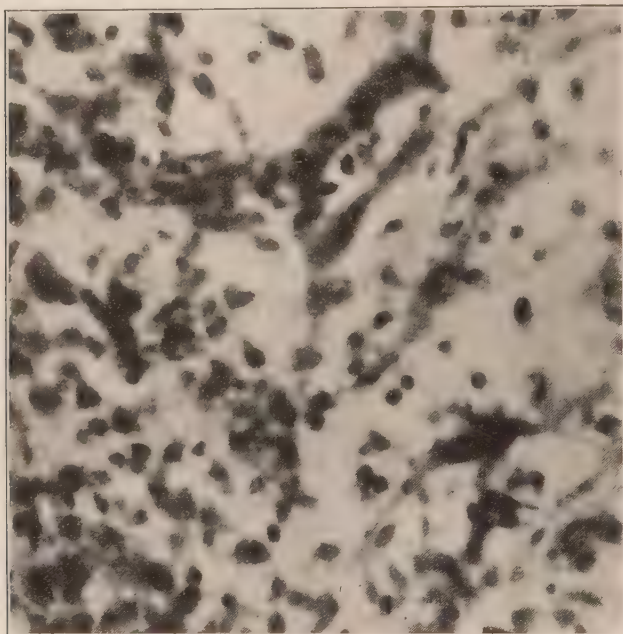


Fig. 62.

The ganglion cells show fairly diffuse degeneration phenomena, most well-marked in the cortex, especially in the frontal convolutions. The cell architecture is on the whole fairly well preserved, but numerous cells show, partly, swelling, chromatolysis, vacuolisation, excentricity of position of the nuclei with shrinking of their membranes; partly, shrinking and irregular outlines, pyknosis, fragmentation, shadow formation. In these areas the glia tissue shows some proliferation of nuclei, some amoeboid cells, and numerous astrocytes, relatively less proliferation of fibers. There are no glia cells of the large, "ballooned", Alzheimer type.

In the basal ganglia and in the pons, the degeneration of nerve cells is considerably less pronounced, showing in these areas no electivity; in the cerebellum (including the dentate

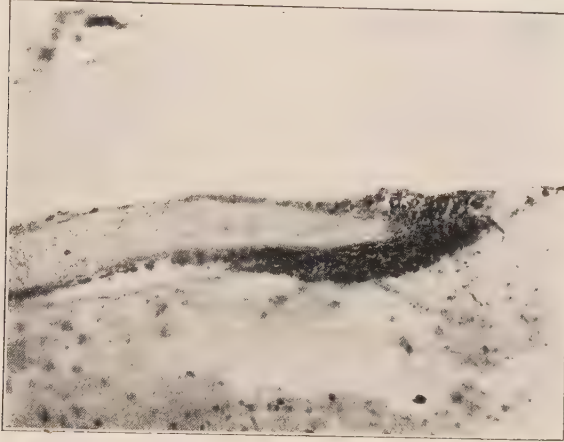


Fig. 63.



Fig. 64.

nucleus) no degeneration can be found, neither in the medulla oblongata

Medullary sheaths preparations from the medulla oblongata show partly some confluent, partly some scattered, patches of degeneration (Fig. 64).

In this patient there is thus on the whole a mixture of more acute and more chronic alterations of vessels and cells, which may very well explain the protracted, remittent-exacerbating clinical picture, including also the striking psychic changes which appeared at a certain period of the disease.

Considering the lack of information during his first hospital stay as to a well-marked lethargic encephalitis, it was quite natural to suppose a more localised and solid brain affection, such as, for instance, brain tumor¹). And it was only the further course of the disease which would lead an observer to abandon this diagnosis and presume the presence of a multilocular, encephalitic process, a view which was supported by the changes in the cerebrospinal fluid.

The following patient was in this department in 1919, before I had taken over the department. The diagnosis of a "disseminated cerebrospinal sclerosis" was made at that time. On perusing the case report at present, and having in mind the knowledge we have more recently acquired as to the clinical pictures of chronic epidemic encephalitis, it is quite easy to see what disease the patient suffered from, more especially, as the clinical picture in reality bore but a slight resemblance to that of the disseminated sclerosis.

Case 62. A seamstress, aged 45, single; under observation in this department from April 4th to December 4th, 1919. She had always been very nervous. The catamenias irregular for the last six months. No severe physical illness previously.

At the beginning of February 1919 she was taken ill rather suddenly, with "disturbances" in the legs; she walked about, however, for some weeks, although she was dizzy and had some falls; at the beginning of March she experienced some difficulty in speaking and swallowing, as if she had a lump in

¹) This patient's epidemic encephalitis must have been one of the earliest cases in Denmark, at any rate the first case in that part of the country, where the "large epidemic" broke out in the following year.

the throat; there was also headache, increased dizziness, asomnia, and dimness of vision. She was admitted to Bispebjerg Hospital 17th March, 1919. According to the case-book of that department she was somewhat restless, "dull", somnolent, seemed to be "far away" when spoken to, had to be fed like a child; in the night she would occasionally cry out and be restless, periodically uncleanly. There was ptosis, no squinting; normal reactions of the pupils and normal eye grounds. Only on one single occasion did the temperature rise, to 38.4°C .

She was now removed to the department for Nervous and Mental Diseases of the Municipal Hospital; here also she was somnolent, answered reluctantly and vaguely when questioned; she seemed indifferent of mood, but not desorientated. Speech drawling, somewhat difficult, not scanning. There was ptosis of both eyelids, no true squint; the upward and downward movements of the eyes were severely reduced, and there was irregular nystagmus on glancing towards the left. The pupils were equal in size, reacting well. No definite defects of the visual fields. Eye grounds normal.

Slight paresis of the left lower facial muscle; the tip of the tongue deviates slightly towards the right: No fibrillation of lips or tongue.

The muscular strength of the arms is somewhat reduced; there is no spasticity. On the finger-to-nose test there is "no true tremor or ataxia, but the index finger will settle on the chin or in the cervical region to be carried slowly upwards to the nose". Distinct adiadokokinesis on both sides, most pronounced on the left.

Abdominal reflexes are present and lively. The muscular power of the legs is reduced, there is no rigidity, the tendon reflexes are brisk with a tendency to clonus; the plantar reflexes are indefinite; on the right side, if anything, it is of the Babinski type. On the heel-to-knee test a similar groping as in the arms is manifest.

She is unable to walk by herself, but has to be supported on both sides; she carries the legs unsteadily, draggingly, without true ataxia, but with considerable swaying and tendency to fall backwards, towards the right; the same is evident when undergoing Romberg's test.

Sensibility, both cutaneous and deep, is intact; as are also the sphincters. There is nothing abnormal about the internal organs. No albumin or sugar in the urine. The temperature was normal on admission. Blood pressure 135 mm.

Spinal puncture: cells $1/3$, globulins 0, albumins 10; Wassermann reaction in serum and spinal fluid negative.

She remained for a long period excessively somnolent, slightly fatuous and babyish. Occasionally there was difficulty of swallowing with regurgitation through the nose of liquid food. Speech continually drawling. She complained of impairment of sight; testing of vision showed 5/18 in both eyes, glasses affording no improvement however; the eye grounds were still normal. Now and again she said that she saw double; the associated vertical immobility of the eyeballs remained very marked.

For some weeks her condition improved somewhat; psychically she became more lively; she could walk better, etc.; then again ensued a relapse, which was now steadily progressive: her speech grew more and more indistinct, drawling, the words drawn out at length, more and more unintelligible; the tone of her voice was described sometimes as "whimpering", sometimes as "wailing"; now and again she had difficulty of swallowing. Frequently fits of spasmodic crying and laughter. All her movements became "flabby and powerless", no possibility of walking except with strong support. Incoordination on the finger-to-nose test. Little by little a considerable rigidity set in in the arms, flexion positions at the elbow joints and wrists, for a period "obstetrical" position of the hands, later, again, the fingers were partly flexed towards the palm. Slight wasting of the small muscles of the hands is mentioned. The rigidity of the legs is said to be less marked than that of the arms; there was however equinus position of the feet. The arm reflexes were brisk, there was bilateral ankle clonus and Babinski reflex, more constant on the right side. The abdominal reflexes were constantly present, although weakened. No disorders of sensibility. Ultimately she became quite uncleanly. The conditions of the eyes seem to have remained unaltered.

After a time her head became drawn strongly forward with contracted sternocleidoids (the head could, however, be made to rest on the pillow). On the left side there were clonic jerking in the sternocleido, in the trapezius and the great pectoral. Gradually also a persistent tremor of the raised head developed, polymorphous of type, a mixture of lateral, forward and backward nodding. There was tremor in the left hand at rest, at a rate of 120 twitches per minute, fairly equal in amplitude, and also a coarse action tremor in the arm, chiefly in the larger joints. The tremor of the head and arms was aggravated by psychic influence, by emotions. The action tremor ultimately amounted to a perfect "motor delirium". No athetoid movements were observed, neither are choreatic movements mentioned.

There was strongly increasing debility and loss of weight. The temperature was taken only exceptionally, being subnormal,

if anything. The liver dulness was not increased. Spinal puncture carried out December 12th, 1919, showed: cells 0, globulins 0, albumins 9.

It is expressly remarked that on trying very patiently to understand the patient's speech, the latter revealed no confusion or distinct dementia.

On December 4th, 1919, she was removed to the Almshouse¹⁾. Immediately on admission, her amimia, her marked speech disturbance ("resembling most a long-drawn howling") were noted; besides, the above described symptoms were evident. After some

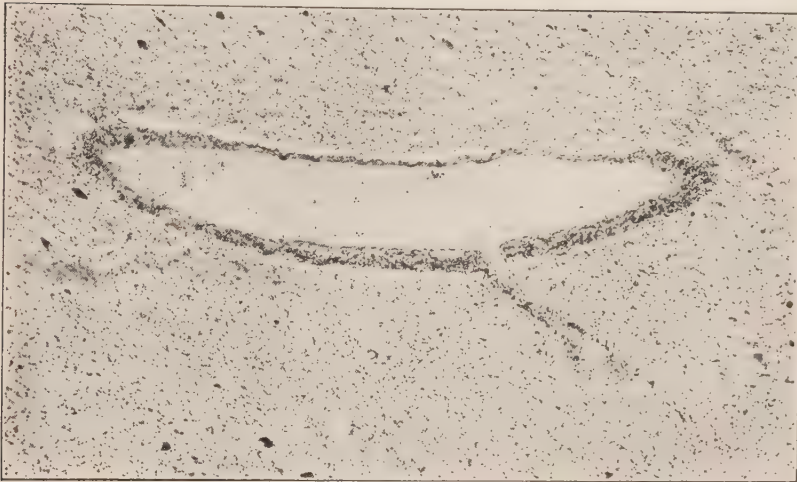


Fig. 65.

time tremor set in also in the legs, occurring synchronously with that of the arms and head. Otherwise the neurological conditions seem to have remained almost unchanged, although with increasing rigidity and contracture of the arms, resulting in total helplessness; in addition, there was some moaning and restlessness. A terminal pneumonia led to her death on July 8th, 1920.

Post mortem examination showed pneumonic processes in both lungs, long-standing pleuritis and fibroma of the uterus.

¹⁾ I am indebted to Dr. Fr. Vogelius, Chief Physician of the Almshouse, for permission to use his report of the case.

The examination of materials from the brain and spinal cord, submitted to us by Dr. Kn. Krabbe, was unfortunately not so comprehensive as we could have wished; some of the material had been lost and what was left had been kept very long in formol.

In the preserved material there were nowhere any sclerotic plaques, no softenings or hemorrhages.

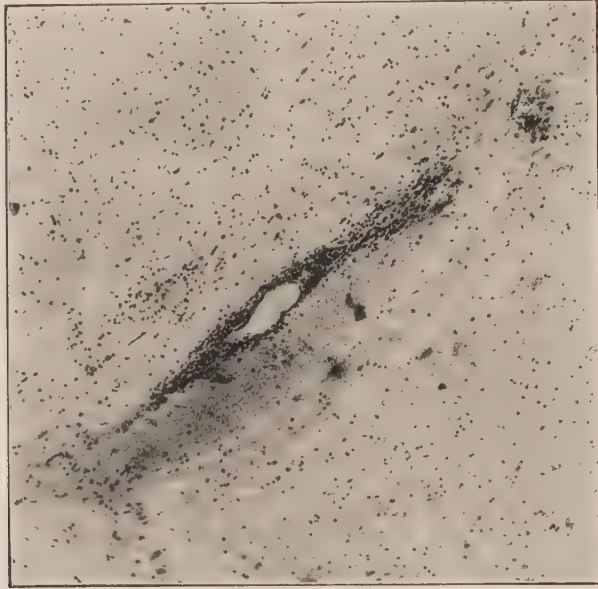


Fig. 66.

In the thalamus, and more especially in the corpus striatum, there were some perivascular infiltrations consisting chiefly of more or less extensive accumulations of lymphocytes (fig. 65); in other places there were exclusively plasma cells. Similar changes, though more pronounced, were seen in the corpora quadrigemina, around the aqueduct, in the pons and the medulla oblongata (Fig. 66). In the cerebellum (including the dentate nucleus) there were no definite perivascular changes. Some few perivascular hemorrhages were found, for instance in the medulla oblongata (Fig. 66).

The nerve cells, judging by preparations with hæmatoxylin, v. Gieson's method, and some not quite successful toluidin-blue preparations, show no marked degeneration or rarefaction

except in the substantia nigra (on both sides) where the nerve cells have almost disappeared, the few remaining cells showing marked shrinking. Staining of the medullary sheaths also gives pronounced degeneration pictures in these parts (Fig. 67). In sections stained with hæmatoxylin fairly marked perivascular infiltrations are seen. The glia tissue shows no coarser alterations.

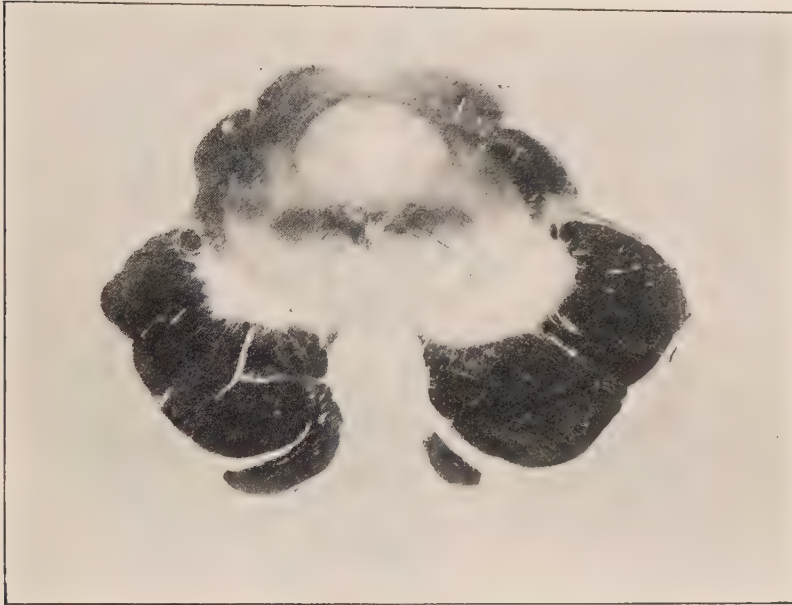


Fig. 67.

Here and there the walls of the vessels are slightly thickened, there is however no distinct calcification of the walls themselves, but outside the vessels, and partly scattered about in the tissue, some roundish or more irregularly shaped calcareous concretions are seen. These alterations are most marked in the pons.

Staining of medullary sheaths reveals, in addition to the above mentioned degeneration of the substantia nigra, a very conspicuous degeneration of the spinal pyramidal tracts; in the cervical cord, too, there is distinct "lightening up" in the anterior pyramidal tracts. This degeneration can be traced all through the spinal cord (Fig. 68), but above the cervical segments of the cord it is completely lacking.

In spite of the imperfect pathologic examination of this case it would seem justifiable to assert two things: a disseminated sclerosis is quite out of the question, and the pathological findings correspond on the whole very

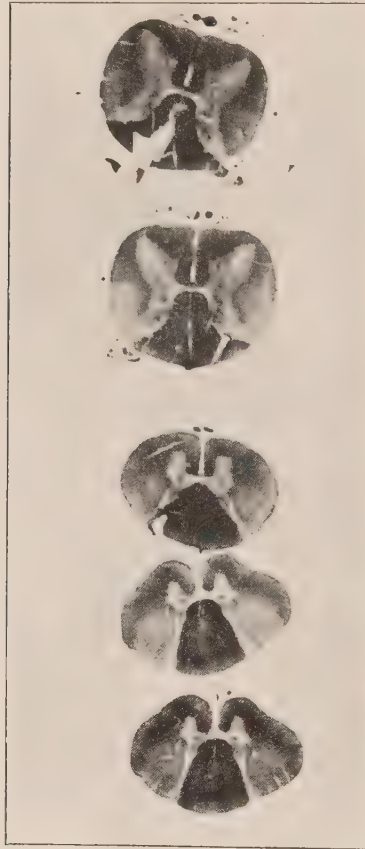


Fig. 68.

well with those of a chronic epidemic encephalitis, a diagnosis which the clinical picture, too, would justify.

Case 63. A woman of sixty-eight, music teacher, admitted 10th October, died 8th November 1923. About eight years previously she went through a rather long period of fatigue, want

of appetite, emaciation, "wan complexion" (icteric?). Subsequent to this she was again as well as ever. During the last 4—5 years she had occasionally had some "fits": for instance, when singing at church she became momentarily "absent-minded", and would cease singing. She had never had any definite epileptic or paralytic attacks.

Three years ago she had "influenza"; slight fever, headache, delirations, light myoclonic jerks in the arms; she remained



Fig. 69.

however up and about, and attended to her work. After that time she felt extremely tired, would fall asleep whenever she sat down to rest a little in the daytime. She had previously had a tendency to be sleepless, but now she slept all through the night, in spite of which she had a feeling in the morning as though she had not slept enough. In the last years of her life her hands began to be shaky; she became "clumsy-fingered", was scarcely able to dress herself, had become "stiff" in the body, with slow movements, felt "poorless". She had also become slow of thought, found it difficult "to translate her thoughts into words", she had to "hunt for the words", but

there was never any paraphasia. Occasionally, she still became absent-minded, or she quite "forgot the time", and was late for dinner. One night she probably lost consciousness, she had fallen half-way out of her bed, and had passed urine involuntarily; on a few other occasions there was also involuntary micturition. Now and again diplopia (she would reach out for the object she believed to see). There were no marked changes of weight, no polydipsia, or polyuria, no loss of hair, no reliable febrile episodes.

She was a woman of a rather strong physique, somewhat lean however, there was nothing presenile about her, no palpable peripheral arteriosclerosis; blood pressure 155/95. Typical

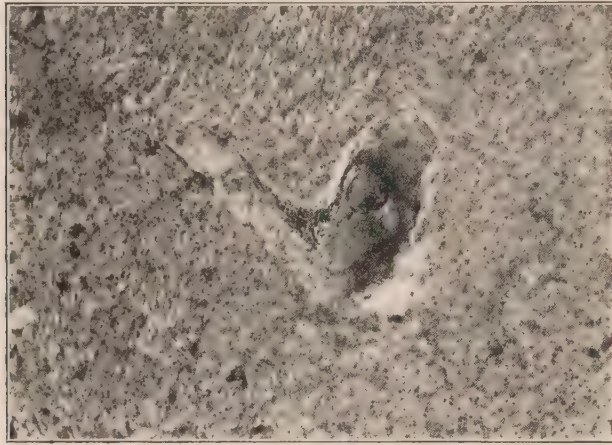


Fig. 70.

Parkinsonian type of face and attitude, some bradybasia, and slight swaying, rather marked hypotokinesia and retropulsion, marked bradykinesia, moderate rigidity of the body, arms and legs, no true pareses, tendon reflexes of the average type, doubtful Babinski reflex on the right side. Slight tremor of the head, coarse, fairly slow, regular, chiefly static tremor of the hands, some rocking and oscillation of the elevated feet. No pronounced bradyphasia, no aphasic troubles. No difficulty of swallowing. No ocular palsies; diplopia cannot be elicited; pupillary reactions, field of vision, eye grounds, normal. No where myoclonic jerking. No albumine or sugar in the urine. Findings in the heart normal: some tendency to tachycardia; the temperature mostly slightly elevated, up to 38.1° in the evenings.

Spinal puncture unfortunately failed, the spinal fluid becoming so mixed with blood that it coagulated at once. Wassermann tests negative

There was no bradyphrenia; she had a good recognition of the "failing of her thoughts" when she wanted to concentrate them. Although clear of mind and well orientated during the early days of her stay, she presently became somewhat clouded, slightly delirious, and confabulating; simultaneously she became more debilitated physically; some râles could be heard in the lungs, and there was a slight degree of icterus, urobiline in the

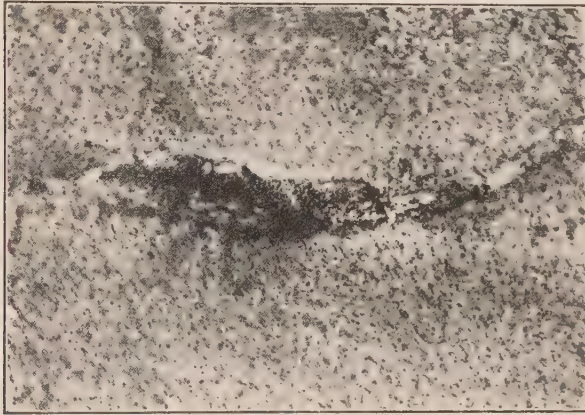


Fig. 71.

urine, tenderness in the area of the gall-bladder. At the same time the temperature rose and, revealing excessive terminal hyperthermia, she ultimately died.

Post mortem examination showed: inveterate tuberculosis of both lungs; a purulent bronchitis, a hemorrhagic infarctus in the left lung, cholelithiasis, chronic fibrous cholecystitis.

The examination of the brain showed no marked sclerosis of basal vessels, nor any meningeal changes or atrophy of cerebral convolutions. The lenticular regions, especially the globus pallidus, had a somewhat indistinct appearance.

The microscopical examination (not yet fully completed) revealed quite definite encephalitic changes in the basal ganglia and the ponto-bulbar region. A number of the small vessels were sparsely covered by plasma cells (Fig. 69) and true perivascular infiltrations with lymphocytes were found in some few vessels in the pons (Fig. 70,71). The Robin-Virchow

spaces were in many places rather dilated, the space being filled up with some few lymphocytes, or, more frequently, with different sorts of débris, showing blue, greenish, or violet stains, whereas only a few granular cells ("Gitterzellen") could be found. The walls of the vessels were rather thickened, assuming a deep red stain when treated by the v. Gieson method, but no calcification could be detected anywhere. Extensive, perivascular hemorrhages were seen in the subthalamic region (Fig. 72).

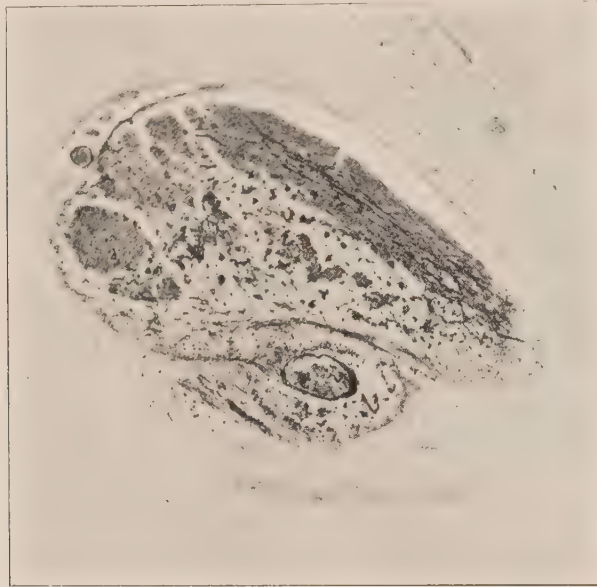


Fig. 72.

In the cells of the substantia nigra degenerative changes were found rather diffusely, viz. pycnosis, considerable increase in content of pigment, fragmentation of the cell bodies, indistinctness of many cells, some being reduced to mere shadows, or a heap of pigment only indicating the former presence of nerve cells (Fig. 69).

Whilst, in the substantia nigra on both sides, these degenerative changes of the ganglion cells were most conspicuous, in the basal ganglia and especially in the globus pallidus, such parenchymatous changes were dubious. Also the perivascular infiltrations, though present in the basal ganglia, were much less marked in these than in the substantia nigra.

In many of the microscopical sections miliary spots of "lightening up" of the tissue were seen, apparently due to rarefaction (or colliquation) of medullary sheaths. In most of these foci, there was a marked proliferation of the fibrillary neuroglia, with the occurrence, now and again, of an isolated astrocyte. On the whole, there was a general process of proliferation of neuroglial tissue all over the parts of the brain examined, but mostly of the protoplasmatic neuroglia, viz. an increase of resting nuclei, some amoeboid cells, some astrocytes, isolated heaps of neuroglial nuclei in a rich mass of confluent protoplasmatic substance.

In the following case the possibility of a disseminated sclerosis had to be considered, although the clinical picture was rather atypical of this disease.

Case 64. Married woman, aged 28, admitted to my department August 30th, 1923. In October 1922 she had an "influenza", with fever up to 37.9° , marked drowsiness, vomiting, dizziness; on two occasions loss of consciousness with "stiffening" of the body. She stayed in bed for two weeks; about a fortnight later she complained of dimness of vision, and during February 1924 she had diplopia for three weeks, the right eye being turned upwards. After the febrile period, she always felt tired, lost in weight, frequently had headache with vomiting, sometimes violent attacks of dizziness. Now and again she would feel rather febrile, had to put on extra clothes during summertime, etc. No polyuria or polydipsia, no disturbances of katamenias. No myoclonic symptoms or the like.

Some eight days before her admittance, she got paresthesias of an itching character in the right arm, which in a few days became weak, so that she could not grasp firmly with the hand. An almost complete right-sided hemiplegia fairly rapidly developed, with a most distressing hyperesthesia ("soreness") in the arm. Then a weakness of the left leg set in. In the neck, the right shoulder, and the right wrist she had rather violent pains.

On her admission, she presented a most marked palsy of the right arm and leg and a slight paresis of the left leg. The face was unaffected, as was also the tongue. In the paretic limbs the tonus was rather increased. Tendon reflexes of the legs exaggerated, with ankle clonus and bilateral Babinski sign. Lower abdominal reflexes absent on the right side. In the right arm and in the legs and in the right half of the abdomen a

marked hyperalgesia and a slight hypoaesthesia were found. She constantly complained of burning or itching paresthesias in the limbs, the trunk, etc., and on the left side of the chest there was an excoriation produced by her scratching herself.

She could not raise her head from the pillow, nor move about in her bed. The cucullares were somewhat tender to pressure. The shoulder joint and right wrist were slightly swollen and very painful on even faint attempts at movements.

Examination of the eyes showed nothing abnormal. No troubles of speech or swallowing. Acoustic and vestibular functions intact.

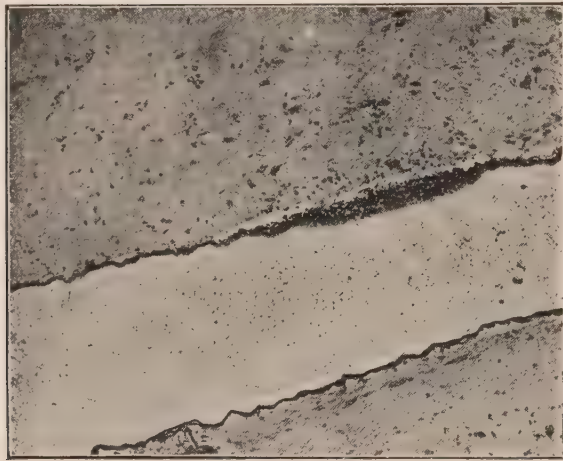


Fig. 73.

During the first period of her stay, there was a marked tendency to retention of the urine. A slight pyuria was observed.

Her condition improved a little during the first month. At the beginning of September, myoclonic starts in the right arm set in and a little later more continuous torsionlike spasms in both arms were seen. At the same time, an arthralgia with some swelling in the left shoulder and a slight paresis of the left upper limb had developed. For a period, too, there were pains and swelling of the right knee joint.

She frequently had attacks of sudden ill-feeling with violent headache and chattering of the teeth, but without rise of temperature or pulse rate. At the end of September and subsequent to such an attack she suddenly developed amaurosis

on the left eye. On ophthalmoscopic examination the macula appeared rather reddish, but no other eye-ground changes were found. Vision of right eye unimpaired. The left pupil slightly larger than the right, not reacting to direct light, the consensual reaction being preserved.

Again, there occurred an improvement in her condition, especially as regards the palsies of the limbs. The arthralgias, and the paresthesias, also improved, the cutaneous sensibility becoming quite normal, while an impairment of the joint sense

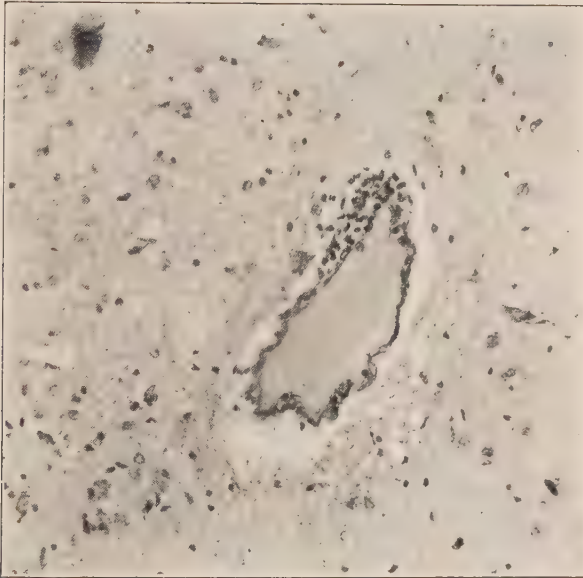


Fig. 74.

in the legs and the right arm was now conspicuous. No true ataxia developed, but there was a marked action tremor in the arms and in these, too, the myoclonic jerks and the slight contorsions persisted. About a month after the setting in of the amaurosis the left eye-ground was found normal and the acuity of vision had risen to 6/12.

X-raying of the right wrist showed a marked atrophy of the small bones. A slight atrophy of the muscles of the left shoulder and of the small muscles of the hands, was likewise found, especially of the left one. The fingers were frequently rather contracted in a semi-flexed position.

At the beginning of 1924, she grew debilitated, the palsies once more increasing, especially in the form of a very strong parapasticity of the legs. She would now and again become a little dyspneic, with low and irregular pulse and slight cyanosis. The examination of the heart and the lungs showed no definite morbid changes. On January 17th, 1924, she had such an attack, without rise of temperature, and this time she did not recover, becoming slightly somnolent, with violent, myoclonic

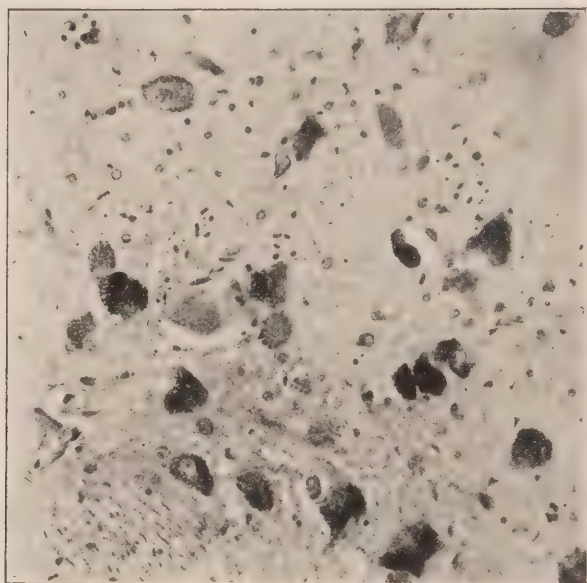


Fig. 75.

jerks and tremor in both arms, increasing cyanosis, strained respiration. The next day she died.

During her whole stay in the hospital, the temperature curve had been rather "flat" until after a treatment with argotropine, when it would sometimes rise slightly, to 37.9° , but, as mentioned above, without showing any connection with her attacks or the other changes in her condition; there was no terminal hyperthermia either. The pulse rate varied somewhat, sometimes rising to 110 a minute, this was the case just before her death. Apart from a passing albuminuria and a slight pyuria,

no abnormal findings in the urine. The spinal puncture, carried out in September, showed: cells 5/3 (lymphocytes), globulins 0, albumins 8. Wassermann reaction negative in blood and spinal fluid.

At the autopsy we were permitted to remove the brain only.

Masroscopically, the brain presented nothing abnormal at all; especially no sclerotic plaques could be seen. Neither in the microscopical examination were any changes suggestive of a true "sclérose en plaques" found.

In most of the sections from the basal ganglia, the ponto-bulbar and bulbar regions, discrete, but quite definite perivascularitic infiltrations were seen, consisting of lymphocytes and plasma cells (Fig. 73, 74); especially, numerous capillaries were found, quite "upholstred" with plasmacells, such being also somewhere seen scattered throughtout the surrounding tissue. The perivascular spaces were a little distended, containing some reddish or greenish pigment. Only a few granular fatty cells could be found. There were no marked sclerotic changes nor calcification of the blood vessel tunics; no endarteritic processes.

The nerve cells were for the most part well preserved, in some few spots showing a slight pycnosis. However, a more extensive degeneration of ganglion cells was not observed, except in the region of the left oculomotor nucleus, in which a number of the nerve cells showed marked degenerative changes, viz. increased pigmentation, chromatolysis, eccentricity of nuclei, fragmentation of dendrites, shrinking and irregularity of cell bodies, some ganglion cells being reduced to mere "shadows" (Fig. 75).

In the basal ganglia, especially in the striatal nuclei, and in the substantia nigra, no such degeneration of nerve cells could be seen.

On medullary sheath preparations and with Bielschowsky staining, no marked changes of medullary sheaths or of axis-cylinders were noticed. Especially no patch-like foci of disintegration.

On specific staining of the glia tissue some general increase of the fibrillary substance was found in a number of sections, most marked in those from the ponto-bulbar region. Nowhere had the proliferation of glia fibers a patchlike arrangement, nor could a "lightening up" be seen on a corresponding section stained with the Weigert method. There was no marked increase in the number of glia nuclei, nor any more marked proliferation of the protoplasmatic neuroglia, though some few "glia swarms" could be found.

Thus, in my opinion, we may consider this case to be one of chronic encephalitis, this diagnosis, too, making the clinical picture more readily understandable.

In acute cases of epidemic encephalitis, the rare occasional occurrence of a meningeal hemorrhage has been mentioned by a few previous observers (Achard, Buzzard & Greenfield, and others), a hemorrhagic cerebro-spinal fluid (Naish), a xanthochromia (v. Economo, Riley) having been observed. In chronic epidemic encephalitis such a lesion seems to be extremely rare. Yet, one would suppose that we might occasionally come across a meningeal hemorrhage in chronic encephalitis also, seeing that degenerative changes of the walls of the blood-vessels are by no means rare in these cases, and that we sometimes find perivascular hemorrhages within the nervous tissue, evidencing a fragility of the walls of the blood-vessels or, maybe, only a tendency to increased diapedesis of the red blood corpuscles. Then, again, if the meninges be especially involved in the encephalitic inflammatory process, as may occasionally be seen, the conditions are suitable for the occurrence of a meningeal hemorrhage. At least, I would suggest such an explanation for the following case.

Case 65. Teacher, unmarried, aged 40, who was admitted to my department January 1st, 1924. He denies a syphilitic infection. He has been excused from military service on account of heart disease, which has, however, caused him no subjective troubles at all. In July 1918 he had an attack of "influenza", lasting for 3 days, with fever up to 39° , headache, vomiting, very marked somnolence. No palsies of the eyes or the limbs, no myoclonic unrest. He had to rise from his bed and attend to his school-work, although suffering still from headache, slight rises of temperature, occasional "darts" in left leg, and feeling very fatigued. At the beginning of September 1918, he became feverish, was somnolent in the day, whilst during night he could not sleep. He was taken to the Øresund Hospital, where he stayed from the 4th to the 23d of September. There was, for some days, a rise of temperature and a tendency to bradycardia (Fig. 76). No true meningitic signs. Sometimes he

„trembled” all over the body. Pupils reacted well; the conditions of the eye-grounds were not examined, nor was any more close neurological examination performed. The urine did not contain albumin or sugar. No abnormal findings in the lungs; in the heart a systolic murmur was heard.

The spinal puncture gave a strongly hemorrhagic fluid, its contents of cells and proteins “corresponding to the admixture of blood”. No bacteria were found.

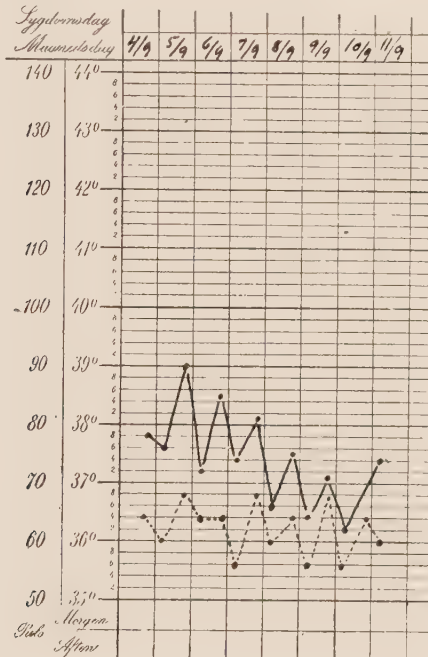


Fig. 76.

After his discharge from this hospital, he took up school-work once more, now and again suffering badly from severe headache with vomiting. On October 5th, 1918, he was found unconscious in the W.C., with a left-sided hemiparesis, and was taken to the Medical department of the Municipal Hospital. He was very somnolent for about 10 days. On the day of admission his temperature was 35.6, rate of pulse 65. Blood pressure 110 mm. There was no biting of tongue. There was a slight anisocoria, the pupils reacting promptly to light, the eye movements being unimpaired, the eye-grounds normal. The hemiparesis seems to have been but little pronounced. A slight

left-sided facial paresis "of the peripheral type" was found, as well as a slight paresis of the left arm, whereas the paresis of the left leg was dubious. Left knee jerk rather diminished. There was a bilateral Babinski reflex.

Spinal puncture, performed on the fourth day of his stay in the ward, yielded a strongly hemorrhagic fluid, which does not seem to have been examined more closely. The pressure of the spinal fluid was found to be 230 mm. Another spinal

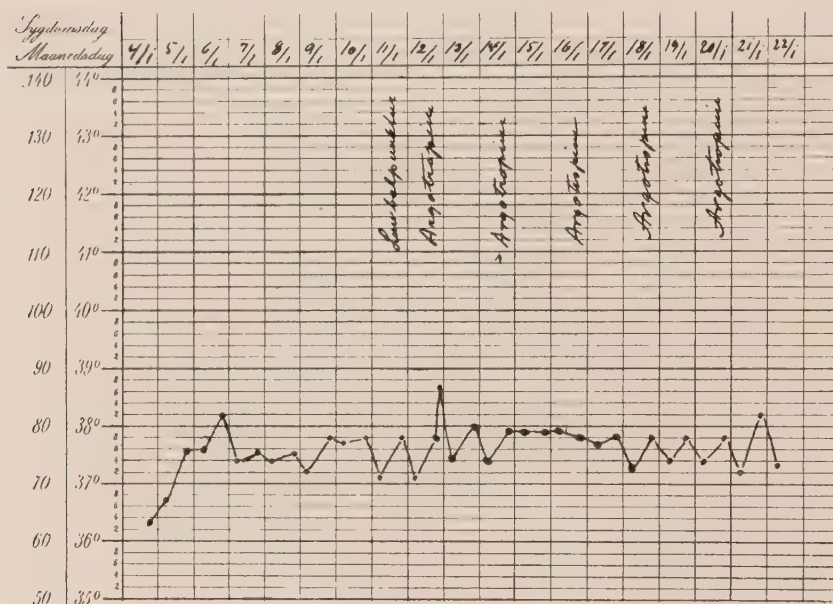


Fig. 77.

puncture on the 16th October produced a clear, yellowish fluid, containing 43 cells (mostly lymphocytes), 3 globulins, 40 albumins. Finally, a third lumbar puncture on the 14th November showed 3 globulins, 30 albumins, the cell figures not being mentioned. The pressure of the spinal fluid was on this occasion found to be 170 mm.

During the first 3 days, his temperature was slightly sub-normal, then, for another five days, it rose to 38.9° in the evenings, afterwards becoming quite normal, like the rate of the pulse. He made a good recovery, so that on his discharge from the hospital, on the 29th of November 1918, he felt thor-

oughly well, the neurological signs having practically disappeared.

He could once more attend to his work, being hampered only by an impairment of his immediate memory, and, now and again, suffering from headaches. Otherwise, none of the usual symptoms of a chronic encephalitis developed, and he had no episodes of fever.

On the evening before his admittance to my department, he was again found unconscious on the staircase of his house. Af-



Fig. 78

terwards, he became somewhat hazy and delirious. There were no spasms, no visible pareses.

In the ward, he was still a little confused, declared he knew nothing whatever of the happenings of the evening before and the night, remembering only, that he had suddenly felt giddy. He complained of severe headache, and a little nausea. The rate of pulse 80, the tension a little low, no irregularity. The temperature $36,3^{\circ}$. Pupils equal in size, promptly reacting to light and on accommodation, eye grounds, visual fields, normal, no impairment of eye movements. No pareses of the face,

the tongue, or the limbs; left-sided ankle clonus, bilateral Babinski reflex. Speech unaffected. No Parkinsonian symptoms, no myoclonias

The spinal puncture, carried out on the 11th of January, produced a rapidly outflowing, yellowish fluid, in which were found about 300 small and mononuclear lymphocytes, together with about 250 red blood corpuscles, 0 globulins, 12 albumins. The Wassermann reaction was negative in blood and spinal fluid. In the urine no albumin, sugar, or blood were found. The

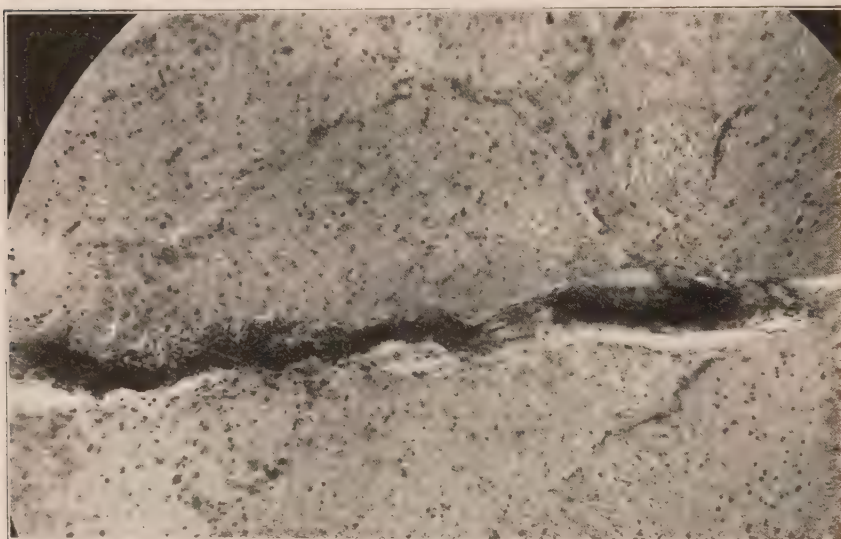


Fig. 79.

findings in the lungs were normal. The examination of the heart showed the presence of a combined valvular disease (aortic and mitral), but quite compensated. X-raying of the heart showed slight increase of the shadow of the heart, but normal shadow of the aorta.

For some days he suffered much from headache and vomiting. There was no longer any true confusion. The temperature (Fig. 77) rose gradually to $38,2^{\circ}$ on the third evening of his stay, after that oscillating, with evening-rises up to $37,8^{\circ}$. Rate of pulse rather varying, from 60 to 80. He was given an argotropine treatment, during which the temperature rose a little more, up to 38° . His general condition improved, the headache and the

vomiting nearly ceasing, the Babinski reflex disappearing. But on the morning of the 22nd of January, he suddenly lost consciousness, became cyanotic, with snoring respiration, clonic spasms in the limbs developed, with increasing cyanosis and weakening pulse. This last attack lasted five minutes. He died at 7,20 a. m.

A spinal puncture, carried out about 8 hours after death, yielded almost pure blood, immediately coagulating.

In this case also, we were only allowed to remove the brain.

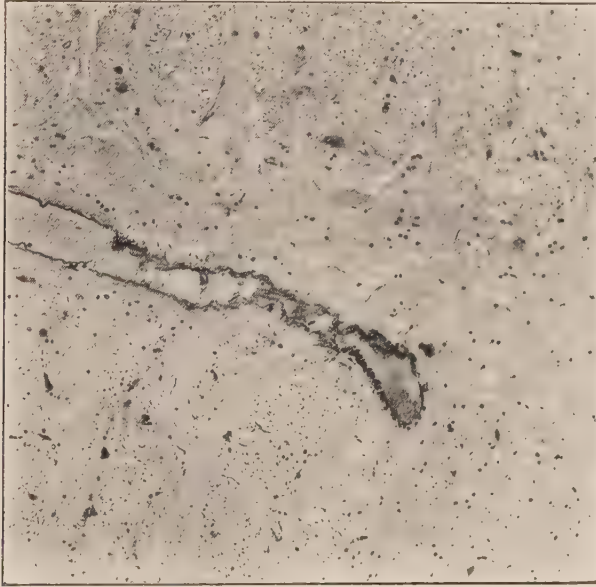


Fig. 80.

The cranial bones, the outer surface of the dura mater did not present anything abnormal. Beneath the dura mater, on the convolutions of the hemispheres, especially the left one, a most extensive meningeal hemorrhage was seen, mostly of a fresh appearance, with clots of newly coagulated blood, blood streaming forth rather abundantly, etc. Around the cerebellum and the brain stem the meningeal hemorrhages were especially pronounced and confluent, the bulbus being imbedded in clots of blood, the spinal cavity, as far as could be seen, being filled up with blood. The bleeding had invaded the lateral ventricles.

On a minute examination of the vessels on the exterior surface of the brain no ruptured aneurysms could be detected, nor any marked arteriosclerosis. There were no macroscopically apparent softenings or hemorrhages demonstrable in gross sections of the brain.

The microscopical examination revealed, firstly, extensive changes in the pia-arachnoid, viz. pronounced perivascular infiltrations with lymphocytes and some few plasma-cells, intermingled with fresh hemorrhagic patches (Fig. 78). Independent changes in the soft meninges, especially proli-

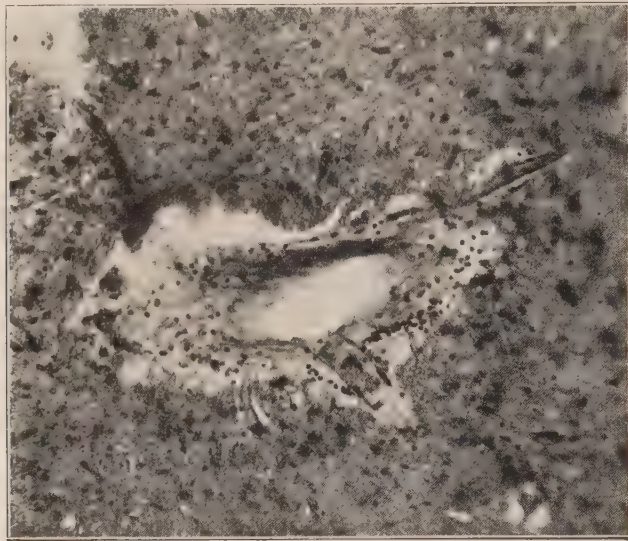


Fig. 81.

feration of connective tissue, were not visible. Only in a few places, did the perivascular infiltrations follow along with the pial vessels into the nerve tissue itself.

Neither in the pial vessels nor in those in the nervous tissue itself were any true arteriosclerotic or endarteritic changes of a syphilitic nature found.

In the lenticular nucleus, in the different levels of the corpora quadrigemina and the pons, in the medulla oblongata, no softening or hemorrhage could be detected. In sections from these parts of the brain definite, though mostly discrete perivascular infiltration was present, made up of lymphocytes and a few plasma cells (Figs. 79—82). Somewhere, for instance

in the nuclei of the tegmentum, a rather large number of the ganglion cells were changed, showing swelling of the cell body, disappearance of Nissl's corpuscles, colourlessness of the protoplasm and the processes, eccentricity of nucleus, fragmentation or even "shadow formation".

In the cerebral cortex the cell architecture was well preserved, and the nerve cells themselves showed no marked pathological changes. Just beneath the cell layer, in the sub-

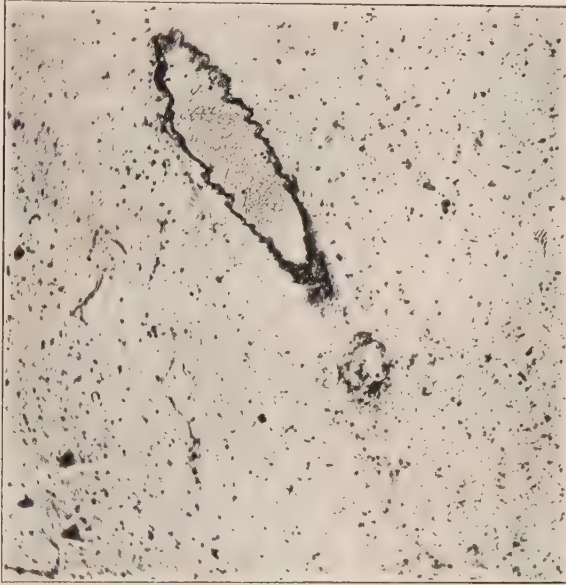


Fig. 82.

cortex, some few perivascular infiltrations with lymphocytes, plasma cells, macrophages, loaded with yellowish pigment, were found.

The glia tissue did not show any marked pathological changes.

I do not intend to enter into a discussion of the etiology of meningeal hemorrhages. Apart from traumatic, toxic and diathetic factors, most observers admit a purely inflammatory genesis, as seen, for instance, in influenza. Eskuchen, some years ago, reported such a case, with

recurring cerebral fits¹). According to Eskuchen, an underlying lesion of the pial blood vessels should always be supposed. In my case, the recurring meningeal hemorrhages of the patient had at least a close chronological connection with his "influenza". Again, a pronounced involvement of the pial tissue and blood vessels was found. In the nervous tissue, itself, reliable, though discrete, perivascular infiltrations were seen, not at all differing from those found in sure cases of chronic epidemic encephalitis.

Although a post-mortem examination of the conditions of the kidneys has not been made, a renal affection can, in my opinion, be excluded, seeing that the clinical observation did not yield any evidence in this direction. As to the heart disease of the patient, I do not think it possible to attach any etiological importance to it at all, seeing that it has lasted from his early youth, without causing any marked troubles and being until his death quite compensated. A syphilitic brain condition, a general paresis or an endarteritic luic affection, must be excluded, the clinical observation and the microscopical examination of the brain offering no proof at all of its existence.

Thus, we are left to suppose an infectious causation of the patient's recurring meningeal hemorrhages, and there is nothing in the clinical picture or in the course of the disease, nor in the postmortem findings, which is not in keeping with an encephalitic infection.

Finally, I shall report the postmortem findings in our Case 13.

Gross sections of the brain did not show any macroscopic changes, especially no softenings or hemorrhages.

On microscopical examination of the cerebral cortex some perivascular infiltrations with plasma cells were seen in the right central lobe (Fig. 83). In one place, together with such infiltrated vessels, softening of the nerve tissue was found,

¹) "Zeitschr. f. ges. Neur. & Psych. 1919, vol. 47, p. 331.

the ganglion cells having almost completely disappeared. The neuroglia tissue did not show any corresponding proliferation. Otherwise, the architecture and structure of the cortical nerve cells were fairly well preserved, especially in the frontal lobes.

In the basal ganglia most pronounced encephalitic changes were found. Throughout all of the ganglia slight perivascular infiltrations with plasma cells could be traced. In the thalamic nucleus, and more especially in the putamen, near to the globus pallidus, some fatty infiltrations were found. An increase

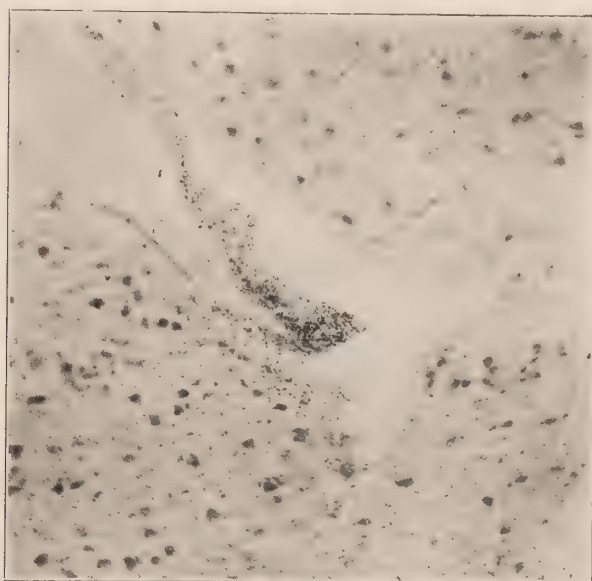


Fig. 83.

in the fibrillary neuroglia was conspicuous in most sections of the basal ganglia, whereas there was no marked proliferation of the protoplasmic glia.

The most profound changes were found in the substantia nigra, approximately of the same intensity on both sides (Fig. 84). Of the nerve cells only a few could be found, the bulk having completely disappeared, leaving only, here and there, scattered heaps of pigment. Pigment was also found in the perivascular spaces. There was, throughout the area of the substantia nigra, a marked proliferation of neuroglia fibers, forming in places a dense entanglement of threads. Around some

of the blood vessels some slight infiltration with plasma cells could be detected on close examination. On sections taken from the substantia nigra with the Weigert myelin sheath staining an almost total disappearance of medullary sheaths was noted.

Thus, in this case, the postmortem findings, especially those in the substantia nigra, agree very well with the clinical picture, this becoming gradually a most pronounced parkinsonism. In addition, one might conjecture a

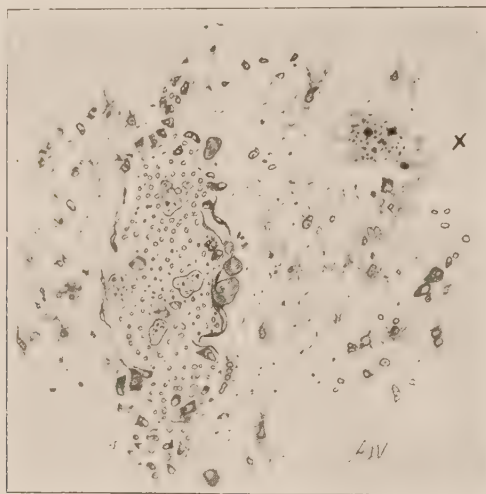


Fig. 84.

At x, a degenerated nerve cell.

“rapport” between the pathologic changes in the right central lobe, amounting to slight softening, and the initial hemiparesis of the patient.

From the postmortem findings in these nine cases as well as from those described in the literature of the subject, we may collect certain main points in the pathological anatomy of chronic epidemic encephalitis.

Very coarse macroscopic changes are rarely found, such as atrophy of the cortical convolutions or basal ganglia, seen in our Case 59, and by Mlle Lévy in a few cases. In spite of the fact that foci of degeneration or disintegration are rather frequently seen under the microscope, macroscopically visible softenings, such as were found in our Case 60, are extremely rare, as contrasted with what is found in Wilson's disease, for instance.

Usually, the soft meninges of the brain are not involved, or are only so to a slight extent. Very occasionally, we meet with a thickening of the pia-arachnoid, a proliferation of connective tissue, appearance of fibroblasts, or the like. Or, again we may encounter a true perivascular infiltration of pial vessels, as, for instance, in our Case 61. A case like our Case 65 stands quite apart as regards the extensive inflammatory changes of the pia and, especially, as regards the abundant meningeal hemorrhages.

Another feature which is characteristic of the histopathology of chronic epidemic encephalitis, is the dissemination of the process over large and functionally different areas of the central nervous system. There is thus not a question of a systematic electivity of the morbid process. At any rate only in as much as the lesions are those of a polioencephalitis, the involvement of the grey matter being predominant in the histopathological picture, and, again, certain anatomically definite areas of the central nervous system being relatively more affected than others.

Evidently, the morbid process is thus usually much more pronounced in the cerebrum (and partly also in the cerebellum) than in the spinal cord, even though changes may also be found here, for instance perivascular infiltrations and degeneration of the ganglion cells in the anterior horns (Fig. 59)¹, more diffuse or more

¹) According to v. Economo this was frequently found to be the case during the epidemic at Vienna in 1919/1920.

funicular degenerations, etc. (Fig. 57,68), etc. Finally, we may meet with inflammatory as well as degenerative processes in the spinal roots (Mingazzini, Schaller & Oliver), and in the cranial nerves (for instance in the trigeminal roots, Mlle Lévy).

Taken altogether, however, the changes found within the spinal cord occur much less frequently, and are considerably less intense than are those found within the brain, the histopathological findings thus differentiating the infectious nerve disease here concerned from the epidemic poliomyelitis.

Within the brain itself we find a relative accentuation of the histopathological processes in certain of the basal segments (cf. below).

The general histopathological picture is that of an inflammatory process, a mesodermic as well as an ectodermic one, showing the simultaneous occurrence of more recent and more chronic histopathological changes: perivascular, exsudative, infiltrative inflammatory phenomena, aggregations of lymphocytes or, in the more chronic forms, especially of plasma cells. Side by side with these changes we have a "parenchymatous inflammation", a degeneration of nervous elements as well as involvement of the neuroglia, etc.

That is to say that the histopathological findings, too, indicate a constantly active morbid process within the central nervous system.

The inflammatory character of the lesion, appearing most conspicuously in the purely lymphocytic infiltrations of the perivascular spaces, may be more or less pronounced; in some cases the inflammatory element is so little evident as to make the histopathological picture appear predominantly as a chronic degenerative process of the parenchyma, of an ectodermic character (v. Economo, Redalié, Trétiakoff & Bremer, Mlle Lévy, Stern, Jacob, Claude & Schaeffer), a difference in regard to the reaction of the cerebral tissue to the encephalitis virus, which is indicated also now and again in more acute cases (Klarfeld, and others).

Quantitatively, at most, the perivascular lymphocytic infiltrations may differ from those found in acute encephalitis; in the febrile relapses (Case 58) they may however attain the same degree of intensity and dissemination as in the acute forms. More usually, however, we find here as in other chronic inflammatory conditions of the central nervous system, a marked addition of plasma cells, upholstering the tunics of the vessels, scattered among the lymphocytes all around the vessel, or, more or less infiltrating large sections of the surrounding tissue without however being en rapport with its vessels. The older and the more markedly "parenchymatous" of character the inflammatory process is, the more will the lymphocytic infiltration be overshadowed by the occurrence of plasma cells.

The true changes in the vascular tunics are of very great interest. We have, here, hyaline degeneration, thickening of the walls, sclerosis, frequently, too, calcification processes (Buzzard, Dürck, Weingärtner, Meggendorfer, Koenig Francais & Lhermitte, Mlle Lévy, Jacob, Mc Alpine, and others).

The same changes may be found in acute encephalitis; thus Spielmeyer found them as early as on the eight to twelfth day of illness¹). Such alterations belong however predominantly to the subchronic or chronic forms of encephalitis, as also evidenced by our cases.

The smaller or minute vessels within the nervous tissue are predominantly or exclusively involved; the changes found often bear a certain focal stamp, being, in my preparations at any rate, most pronounced in the basal ganglia (Case 59).

Usually, the intima was found to be intact; an intima proliferation, such as seen for instance in certain syphilitic vascular affections (the Nissl-Alzheimer form), or true obliterating endarteritis have not been evident in any of my preparations.

¹) Histopathologie d. Nervensystems. Berlin 1922. Bd. 1. p. 219.

The hyaline (colloidal) degeneration seems principally to involve the adventitia, to a lesser extent the media (Fig. 51); here, too, are seen the first precipitations of calcareous particles. As far as the capillaries are concerned, the calcareous particles are found in the perivascular spaces. And, as seen in my case 59 (Fig. 46), swarms of larger or smaller, roundish or irregularly shaped calcareous concretions will frequently be emitted from these spaces out into the tissue¹).

No more pronounced changes in the elastic membranes were evident in my cases.

The thickened, stiff small vessels seem sometimes to be "coiled up" like a rope, so that the lumen of one and the same vessel appears several times in one section. Neoformation of capillaries, such as is found in syphilitic processes, or secondary canalization of obliterated vessels, were not seen.

These chronic vascular changes correspond very well with the progressiveness which, in spite of all oscillations, nevertheless characterises most cases of chronic epidemic encephalitis. Buzzard was one of the first observers who supposed a connection between the vascular affection and the symptoms occurring at a later stage of the disease.

Not at all or only in some few cases (Fig. 66, 72) do these vascular changes lead to hemorrhage, thus distinguishing themselves essentially from those of true arteriosclerosis or of influenzal encephalitis. At least, the "annular hemorrhages" (Flohstich Blutungen) of the influenza encephalitis were never seen. On the other hand, a case like

¹) When speaking above of calcareous particles and concretions, I would not venture to assert that the terms are absolutely correct; perhaps there is a question only of preliminary histo-chemical changes, the true calcareous infiltration occurring later on (Aschoff, v. Gierke, Perusini, Spielmeyer, Lhermitte, Walter Kraus & Mac Alpine). The particles here described assumed a deep blue stain with Nissl's method and with hematoxylin; unfortunately, however, they were not subjected to any of the finer chemical staining tests.

our Case 59 shows that thromboses may occur, a condition which was also found frequently by Buzzard & Greenfield in acute encephalitis, and which, perhaps, in connection with a flashing up of the exudative inflammatory processes might account for the occurrence of certain clinical symptoms of an apoplectiform onset.

The adventitial spaces are often found to be excessively dilated. This may of course be an artefact. But, more usually, the walls of the vessel in question show chronic changes, the adventitial space being packed with pigment cells, macrophagocytes, calcareous concretions, disintegration products of other kinds, etc. And, more especially, perivascular parenchymatous degeneration foci are frequently found in the surrounding nervous tissue (often in connection with spongy proliferating neuroglia, fig. 48). The tissue in question may remind one of the senile or arteriosclerotic "*état criblé*", just to the point of the formation of small lacunes (Mlle Lévy, Henry Marcus).

A diffuse and apparently independent degeneration of ganglion cells is of frequent occurrence in chronic epidemic encephalitis, as is also evidenced by our cases.

The histopathological pictures of these changes are identical with those known in other cerebral affections, except that the chronic affections of the cells (Nissl), such as shrinking, sclerosis, pycnosis, fragmentation, "shadow"-formation, etc., are more prominent than for instance swelling, chromatolysis, etc. The disturbances of the general architecture of the cell layers, which is so characteristic of the brain lesions of general paralysis, is at any rate not the rule in chronic epidemic encephalitis.

The affection of the cells will often attain a special massivity in certain of the basal parts of the brain, such as the corpus striatum, and strikingly frequently in the locus niger (Trétiakoff & Bremer, Lhermitte, Foix, Marinesco, Goldstein, Jacob, Claude & Schaeffer, Spatz, F. Stern, Mc. Kinley, Mc Alpine, Henry Marcus; see also our

Cases 62, 63, 13). Whether this should be taken to indicate a special "electivity" on the part of the cerebral sections named, and not merely that they are also the places of predilection for the mesodermic inflammatory processes, will be discussed later on.

The neuroglia tissue is more or less involved in the morbid process, predominantly in connection with exudative or parenchymatous inflammation. We find proliferation with the appearance of amoeboid cells, astrocytes, glia throngs and glia nodules (Fig. 43,52), and, finally, a more or less profuse proliferation of glia fibers, surrounding or interlacing for instance foci of parenchymatous disintegration, sometimes like a dense "felt", sometimes of a more spongy appearance (v. Economo, Schaller & Oliver). The more massive glia proliferation which leads to the formation of the sclerotic "plaques" in disseminated sclerosis, are not found in chronic epidemic encephalitis. Neither do we find that abundance and polymorphism in regard to proliferation of nuclei and protoplasm which is seen for instance in general paresis.

In none of my preparations did I find the "ballooned" glia nuclei of the Alzheimer type which are so characteristic of the histopathological picture found in Wilson's disease, in pseudosclerosis, and in certain forms of torsion spasm (Thomalla, Wimmer).

Several writers mention neuronophagia in connection with chronic epidemic encephalitis. In my own cases numerous satellites and other forms of glia cells were frequently seen surrounding the degenerated ganglion cells. In by far the majority of cases, however, the picture will be more readily interpreted as a necrophagia (Marinesco) very similar to what I found in my case of pseudosclerosis.

In connection with the perivascular infiltrations, the vessels that have undergone chronic changes, or the parenchymatous degeneration foci, various products of disintegration are often found in abundance: pigments,

lipoids (Fig. 53), amylaceous bodies (Fig. 46), etc., either scattered about freely, for instance in the adventitial spaces or in the glia stroma, or in fatty granular cells, gliogenous "Gitterzellen", etc. These changes present however nothing that is specifically characteristic of chronic encephalitis; they are found in a far more pronounced degree in other chronic affections of the central nervous system.

Specific staining of medullary sheaths often reveals degenerations. Sometimes only as a "lightening up" of the interlacings of the medullary sheaths, a partial Marchi-degeneration, for instance in the nucleus ruber (Case 60), or in areas where Nissl's staining method shows parenchymatous degeneration or perivascular infiltrations. On other occasions we find larger, unsystematised fields of degeneration, for instance in the medulla oblongata (Case 61), reminding one macroscopically of the "plaques" in disseminated sclerosis. This degenerative process does not only involve the medullary sheaths but also, and to as great an extent the axis-cylinders, as shown in the preparations with Bielschowsky's method.

Of peculiar interest are the more or less well-marked funicular degenerations, such as are found in Case 62 (areas of the pyramidal tracts) and in Case 60 (posterior columns, crus cerebelli ad pontem).

v. Economo, and more recently Hedinger, Mlle Lévy, Stern, Mc Alpine, have described such funicular degenerations. In one of Mlle Lévy's cases there was, however, a more diffuse degeneration in the antero-lateral segments of the spinal cord.

Whether in these cases of ours, as well as in those described by other writers, there is actually a question of a primary degeneration and one that is restricted to a definite anatomical and physiological system, it is as difficult to decide in regard to cases of chronic epidemic encephalitis, as in the combined funicular degenerations in pernicious anemia, Erb's syphilitic spinal paralysis, etc.¹⁾

¹⁾ Wimmer: Die syphilitische Spinalparalyse (Erb.) Deutsche Zeitschr. f. Nervenheilkunde 1907. Bd. 32. 308.

The apparently pronounced "electivity", for instance of the pyramidal tract degeneration in our Case 62, might tempt one to think of a toxic action, the toxin showing thus a special affinity for certain nervous tracts. In Case 60, however, mild perivascularitic processes were found in the degenerated areas of the posterior columns; in Case 58 the pyramidal tract area in the medulla oblongata showed similar alterations, although there was no visible degeneration of the pyramidal tracts themselves in the Weigert-Pal preparations. In Case 62, moreover, we have the peculiar feature that the degeneration of the pyramidal tracts is checked above the cervical portion of the cord, which would be rather incomprehensible if there was a question of a "systematic" degeneration process.

Here as well as in regard to anemic and syphilitic funicular degenerations, one might be inclined to suppose that the funicular degenerations are in fact due to a coalescence of more limited areas of tissue degeneration, in combination with true inflammatory processes, following the distribution of the vessels, the "systematisation" being furthermore emphasised by the addition of ascending and descending secondary degenerations. At the present time, however, it is hardly possible to decide which of the two interpretations of the funicular degeneration is the correct one.

Neither can it be ignored that the same uncertainty prevails in regard to the question of the primary nature of the changes which we have designated as parenchymatous degeneration of ganglion cells. It is quite certain that the affection of the ganglion cells is often strikingly diffuse, and, like the more restricted parenchymatous tissue degeneration, it very often does not show any definite topographical connection with the vessels or with the exudative inflammatory processes. This apparent lack of connection might however, in some cases, be due to the fact that the areas in question have not been examined in serial sections. And, again, in the massive degener-

ation of ganglion cells seen in the substantia nigra of our Cases 13, 62 (and 63), we found correlated, although vague, perivascular infiltrations, a coincidence which has also been witnessed by Français & Lhermitte, Marinesco, Mlle Lévy, Mc. Kinley, Henry Marcus, Mc Alpine, in their cases of ("elective") degeneration of the locus niger.

In chronic epidemic encephalitis we are thus confronted with the same problem as for instance in general paresis, in regard to which, as is well known, it has been the subject of wide discussion.

Mlle Lévy states that in her four autopsies (cases of parkinsonism) she did not find any changes in the spinal ganglia, the sympathetic ganglia, or in the muscles.

In the endocrine glands, any very marked morbid changes seem to be of rare occurrence. Neither v. Economo, Marie & Trétiakoff, Marinesco, Mlle Lévy, nor Jacob, found any changes in the hypophysis. In the suprarenal glands Marinesco found perivascular infiltrations of lymphocytes and plasma cells, more especially in the medullary substance.

Marinesco also found marked inflammatory changes in the parotid gland, as also did Netter.

In our Case 60 the liver was examined; neither macroscopically nor microscopically did it present anything abnormal, especially nothing suggestive of the hepatic changes found in the hepato-lenticular degeneration. Jacob found signs of stasis and fatty degeneration and some slight lymphocytic infiltrations. As to the most interesting case of Westphal & Sioli, I should not think the diagnosis sufficiently sure to make it a conclusive proof of the existence of a true encephalitic cirrhosis of the liver.

PATHOGENESIS.

According to the results of experimental investigations on epidemic encephalitis (Strauss, Hirschfeld & Loewe, Levaditti & Harvier, Mc. Intosh & Turnbull, Kling, Davide & Liljenkvist, Thalhimer) it must be considered an established fact that, quite apart from its epidemiological relationship to influenza, epidemic encephalitis is an infectious disease *sui generis*¹⁾.

Its pathogenic noxa is an invisible, filterable virus ("ultra-virus"), extremely resistant to glycerine, desiccation, heating (to 55°); it keeps virulent for long periods in water and milk, it can be destroyed by carbolic acid and permanganate of potash.

Experimentally, the virus can readily and reliably be transmitted to rabbits by intracerebral inoculation or inoculation on the cornea of the animals (Levaditti & Harvier); in the latter case the virus will very rapidly transverse the vitreous and travel along the optic nerve to the brain. The virus may fairly readily be transferred from the first infected rabbit to other rabbits, and may often be held virulent through several animal passages.

In the rabbit brain, after varying intervals (cf. below), the virus will produce acute or more chronic changes, quite corresponding to those found in the human brain (cf. Fig. 38, 39); Levaditti did not find any alterations in the spinal cord of his animals.

In the organism of encephalitis patients the brain is obviously the most likely place to look for the virus.

¹⁾ C. Levaditti: *Ectodermoses neurotropes. Poliomyélite-Encéphalite-Herpès*. Paris 1922.

Less frequently do we obtain positive results from inoculation of the cerebro-spinal fluid into rabbits (Levaditti & Harvier, Schnabel), such as in our Cases 28, 36, 46)¹⁾. Successful inoculation experiments on monkeys and rabbits have also been carried out, however, with secretion from the nasopharynx (Bradford, Bashford & Wilson, Strauss, Hirschfeld & Loewe), with saliva (Netter), and with intestinal contents filtered through a Berkefeld filter (Kling, Davide & Liljenkvist); whereas the virus is very rarely found in the blood of the patients²⁾.

Of special interest is the occurrence of the virus in the naso-pharynx and in the saliva, partly in encephalitis patients, and partly also in healthy individuals, that is to say in persons who have never clinically presented any symptoms of encephalitis or persons who, at most, have suffered from non-specific catarrhal, gastro-intestinal, rheumatoid attacks, or the like (Kling). Thus we have here the same category of healthy carriers as in so many of the other infectious diseases, for instance in the epidemic anterior poliomyelitis (Wichmann).

Experimental as well as clinical observations tend to show that the virus can remain active for very long periods in the infected human organism, as in fact Netter had already asserted at an early stage of the investigations into this disease. In inoculation experiments on rabbits this author was able to demonstrate active virus in the brain substance from a case of encephalitis of five months' standing. He tells of another patient who had a mild rhythmical muscular unrest as the sole "remnant" of an encephalitic attack, but who, two years after its onset, developed a diplopia, and who, at the same time, transmitted the disease to his father. Lemierre

1) Pette, also, did not obtain positive results from such inoculation experiments.

2) The question regarding the identity of the virus of encephalitis epidemica with that of herpes (Doer, Schnabel, Levaditti, and others) can here presumably be left out of consideration.

mentions a transmission of the infection from a case of three years' standing. In their animal experiments Levaditti & Harvier find the virus to be active for as long a period as six months, Kling, Davide & Liljenkvist for as long as eight months after the onset of the disease.

The inoculation experiment in our Cases 28, 36, 46, the frequently very long interval between the initial infectious phase and the relapses, as seen, for instance, in our Case 58, also distinctly evidence the tenacious persistence of the virus within the infected organism.

The experiments, the epidemiological observations, the clinical picture as well as the pathological findings, thus tend to show quite clearly that as regards the nervous affections we are concerned with here, it is not a question of "sequels" to an acute infectious process, but of a chronic specific inflammatory process in the central nervous system. This is true, at any rate, in by far the majority of cases.

This chronicity of the action of the virus in the central nervous system has caused several authors (Stern, v. Economo, and others) to speculate upon whether these chronic processes were to the same extent as the acute ones the manifestation of the specific action of the virus in the nervous tissue¹). Similar considerations as those which have for a long time been advanced in regard to the "metasyphilitic" affection, the general paresis, are met with here. In order to account for the interval between the infection and the cerebral affection, and to explain its chronicity and histopathological picture (more especially perhaps the "parenchymatous inflammation"), it has been thought necessary to insert pathogenetic intermediary links between the spirochetes and the cerebral changes in question; Kraepelin's supposition of "intermediary metabolic disturbances" is thus well known; also the theories of Hauptmann²).

¹) As to Sicard's "paraencephalitis", compare p. 301.

²) *Zeitschr. f. ges. Neur. & Psych.* 1921. vol. 70. p. 254.

In the case of general paresis, however, spirochetes have actually been found, often in abundant masses, in the cerebral tissue; in chronic encephalitis we only know that a virus exists; this is evidenced, among other things, by the animal experiments. In view of this knowledge, I think a direct action of the virus on the surrounding brain tissue is the assumption most supported by facts. Peculiarities in the virus itself (attenuated virulence, etc.) or in the infected organism (protective reactions) might account for the chronicity of the clinical and histopathological pictures; this question will be further dealt with below.

F. Stern has been especially impressed by the fact that, under the influence of the encephalitis virus, chronic nervous affections are seen to occur in "giant series", affections which, apart from some semiological variation of minor importance, are of a strikingly uniform symptomatological type, being, in by far the majority of cases, a parkinsonism with more or less pronounced vegetative disorders, the anatomical substratum of which, according to our present knowledge, should be sought for in the striatal parts of the brain. To account for this "electivity" the author considers it necessary to suppose extracerebral co-agents for the occurrence of the chronic epidemic encephalitis.

For the present I will only say that even though the extrapyramidal syndrome (parkinsonism, hyperkinesia) constitutes a predominant feature in the picture of chronic encephalitis, other symptoms and syndromes are also frequently met with. Stern finds it surprising that the chronic encephalitis process in by far the majority of cases leaves the brain stem free, that is to say just those cerebral sections which are preeminently the seat of the changes in acute encephalitis; but this cannot be said to be correct, either clinically or pathologically; at least, there is no absolute "refractivity" on the part of the brain stem against the encephalitis virus as soon as the affection becomes chronic. And, moreover, this in-

susceptibility on the part of the brain stem during the further chronic development of the disease might perhaps be due to a local immunity, an insusceptibility of the tissue itself having occurred subsequent to and coincident with the healing of the acute changes.

Apart from the "electivity" (in regard to which Stern considers it justifiable to exclude a localising influence through the vascular system of the basal ganglia of the brain), it is the quite dominating degenerative changes which frequently occur in the nervous system, the changes in the blood picture, the vegetative and endocrinal symptoms, and the like, which cause Stern to suggest extracerebral, hematogenic co-agents as inducing the chronic encephalitic changes, a toxic or fermentative noxa destructive to the cerebral tissue, circulating with the blood. He draws a parallel with the conditions found in poisoning caused by carbon monoxide or manganese¹⁾; in Wilson's disease with the pronounced hepatic affection; in the cerebral affection following on poisoning with guanidin (Fuchs), or, again, on the elimination of the hepatic blood circulation (Kirschbaum, and others). Such circulating noxæ might be thought to occur, in chronic encephalitis through an affection, for instance of endocrine organs, of the liver, etc.

Mourgue²⁾ puts forward similar considerations, in regard, partly, to "the extrapyramidal syndromes" quite generally, being evidently from the first inspired by Crile's theories on the protective functions of the liver to the advantage of the brain, more especially against acidosis and deficient sugar production.

A. Fuchs, by subcutaneous injections of guadinin into cats, has been able to produce a "guadinin encephal-

¹⁾ F. H. Lewy & L. Tiefenbach: *Zeitschr. f. ges. Neur. u. Psych.* 1921. Bd. 71, p. 303.

²⁾ Le syndrome clinique de la rigidité décérébrée de S. A. K. Wilson étudié dans un cas de spasme de torsion consécutif à l'encéphalite épidémique. *Arch. suisses de neur. & de psych.* 1922. vol. XI.

opathy" which, in Pollack's microscopical examinations, appeared as diffuse inflammatory processes, principally in the basal ganglia of the brain, in the pons, the medulla oblongata, the dentate nucleus of the cerebellum. What is of interest to notice here, is that the changes were more pronounced the more chronic the intoxication had been. The animals showed choreiform muscular unrest. Also by establishing an Eck's fistula in dogs Fuchs obtained "encephalitic" changes, the occurrence of which was supposed to be due to metabolic "slags" which the liver had not been able to destroy.

Quite recently, Kirschbaum, in some papers¹⁾, occupied himself with the effects of severe injuries of the liver, elimination of the hepatic blood circulation, guanidin intoxication of the central nervous system. Kirschbaum calls attention to the theories advanced by some French and a few German writers in regard to the connection between a disturbed hepatic function and certain psychic affections, mentioning, moreover, the very peculiar cases described by v. Voerkom and v. Economo-Schilder, i. e. extrapyramidal syndromes and psychic disturbances in patients somewhat advanced in age suffering from interstitial hepatitis and diffuse degenerative cerebral changes, of a cortical localisation, but also of the basal ganglia and the cerebellum. In this connection the author of course also mentions the hepatic-lenticular degeneration. He himself records three cases of acute icteric atrophy of the liver. The clinical picture of these cases bore no striking resemblance to the classic lethargic encephalitis. The pathological findings were: diffuse degeneration of ganglion cells, proliferation of glia cells, fatty degeneration of the vessel tunics, but no exudation or infiltration processes; that is to say, a histopathological picture which in fact is hardly suggestive of epide-

¹⁾ Ueber den Einfluss schwerer Leberschädigungen etc. Zeitschr. f. ges. Neur. & Psych. 1922: Bd. 77. S. 536, and XII. Jahresvers. Gesellch. deutscher Nervenärzte. Ref. Ztrbl. f. ges. N. & P. 1922 Bd. 30. S. 404.

mic encephalitis. Kirschbaum also emphasizes the fact that there was no elective involvement of the ganglia of the brain stem. Neither in his animal experiments did the author find any exclusive or dominant involvement of the striatum or the pallidum.

For the present, the safest conclusion to draw from these and similar investigations will be that also in regard to hepatic injuries (in the most comprehensive sense of the term) the cerebral tissue shows prompt and intense reaction, such as it does to nearly all the infectious noxæ, for instance. The only reliable datum we have to go by at present, as far as this matter is concerned, is the purely clinical fact of the simultaneous occurrence of a hepatic and a cerebral (although not even elective) affection in the so-called hepatolenticular degeneration. That there should be any pronounced phylogenetically or biochemically conditioned "elective affinity" between certain abnormal metabolic products, toxins, bacterial products, and the like, and the basal ganglia of the brain (Fuchs, Lewy, v. Economo, and others) may be possible, but, so far, it is only a hypothesis. I should therefore think it a little premature when Mourgue asserts that the extrapyramidal syndromes (including the encephalitic ones) "*constituent des affections du métabolisme général des matières protéïques. Les syndrômes dits extrapyramidaux paraissent être des maladies de l'organisme tout entier*"¹).

In his patient with encephalitic torsion spasm, who did not present any of the more common clinical signs of hepatic affection, Mourgue thinks it justifiable to conclude an impairment of the liver function, on the basis of the findings of alimentary glycosuria, urobilinuria and bile pigments in the blood. Meyer-Birch & Stern also state that they have found signs of disturbed liver func-

¹) To Buscaino, too, the "complicating" degeneration of the nervous tissue is due to circulating toxic substances, viz. abnormal amines, absorbed from the intestinal tract (*Giornale di Clinica Medica*. Fase I. 1924).

tion in chronic encephalitis¹⁾, i. e. urobilinuria, hyperglycosuria following on the administration of large doses of levulose.

That in chronic epidemic encephalitis we find clinical symptoms which may be understood as indications of metabolic disturbances is quite certain, and has been pointed out previously in this work (p. 27). Thus, for instance, the frequent occurrence of disturbances of the neutrality regulation in our encephalitic cases might be taken as an indication of changes of this kind. Whether these changes however are of endocrinal origin or perhaps due to morbid changes in the functions of the liver, or to toxic substances, resorbed from the intestinal tract (Buscaino) or, finally, depend on lesions of central sympathetic centres, we had better leave an open question for the present; compare below p. 311.

The organic changes which lead to these "metabolic" disturbances in chronic epidemic encephalitis might, however, very well be thought to run parallel with the primary cerebral changes. As being more probable than a direct and elective, "destructive" toxic effect on the nerve tissue of these metabolic "slags" (Fuchs), or an endogenic protein toxicosis (Stern), I would suppose an interaction of a somewhat different kind: the abnormal metabolic products in question might be thought simultaneously to alter the biological modes of reaction of both the virus and the nerve tissue, for instance, in such a way that the tissue reaction following directly upon the presence of the pathological germs, i. e. the inflammatory process s. s., the mesodermal reaction, would become more or less overshadowed in the histopathological picture by a more toxic-chronic degeneration of the extodermal cerebral tissue. The chronic encephalitic changes would then, nevertheless, first and foremost be due to the action of the encephalitis virus in loco.

¹⁾ Klin. Wochschr. 1922. S. 1559.

That this action, histopathologically as well as clinically, is so varying in its aspect, ranging from an acute fulminating to a chronic insidious mode of manifestation, should no doubt be attributed, also, to specific biological properties of the virus transmitted, as well as of the organism which harbours it. In this respect the animal experiments are of interest. Rabbits are, as a rule, rather susceptible to the encephalitis virus; monkeys are almost immune; monkeys may however show themselves susceptible to a virus which has been made more virulent by passage through rabbits. While in the experiments of Levaditti & Harvier, the incubation period of the virus took a few days only, the changes produced having the character of acute encephalitis, Kling, Davide & Liljenkvist just point out the protracted period of incubation up to from two to four months, and more especially the predominantly chronic character of the histopathological changes brought about in their rabbits. Another observation made by these authors, and by Thalheimer, is also of very great importance, namely that the inoculated virus need not produce microscopically visible changes in the brain of the rabbit first inoculated, while inoculation into a second rabbit of the cerebral substance of the first one, produces encephalitic changes, such as it was also found in our inoculation experiment with cerebrospinal fluid.

It is therefore a rather likely supposition that the virus can "vegetate" within the central nervous system (virus cagé, Netter) without producing any true mesodermal reaction (perivascular infiltrations), but only miliary insidious degeneration processes, which may exist for long periods without manifesting themselves in pronounced clinical symptoms, and perhaps also without being sufficiently massive and extensive to become detectable under the microscope.

I should not omit to mention a rather original theory which has been advanced by Sicard¹⁾, in regard to cases usually included under the heading of chronic epidemic encephalitis.

Sicard states that, in addition to the "true" epidemic encephalitis, we have "para-encephalitic" affections, as we have, for instance, para-typhoid. According to Sicard, clinical experiences show that the "true" encephalitis virus, in at least two thirds of the cases, breeds a parkinsonism; whereas the "para-encephalitic" infections never give rise to that morbid condition.

Among the "para-encephalitic affections" Sicard enumerates epidemic hiccough, the chorea of Sydenham, the spasmodic torticollis of Brissaud, and "recurring mesocephalitis".

Now, as regards Sydenham's chorea, I would agree with Sicard, believing it to be an infectious disease on its own. Of epidemic hiccough, some few remarks have been made already (p. 73), to the effect that both epidemiological and clinical facts tend to prove it to be a true encephalitis affection. As to the spasmodic torticollis, I do not think that we have, as yet, sufficient clinical and anatomical evidence to decide the question. Only so much can be said that, in several instances, the wry neck ran along with true encephalitic manifestations.

Judging by the clinical picture of the cases of "recurring mesocephalitis", as briefly described by Sicard, these cases do not differ essentially from some of my intermediary cases recorded above. Then, again, in these "mesocephalitic" patients we may encounter slight or more marked signs of parkinsonism, etc., so that, in my opinion, a purely clinical distinction is quite impossible.

Finally, we have the identity of pathological findings in the cases of parkinsonism and those of other clinical types.

¹⁾ Journal médical français. 1923. p. 140.

I should not venture absolutely to refute the conception of "para-encephalitic" morbid conditions; only, at the present stage, this conception lacks bacteriological and serological proofs. And from a purely clinical and anatomopathological point of view such a differentiation does not seem to me to be needed.

In this work we have several times been confronted with the question: relapse or reinfection? The reply to this query depends to a great extent upon the answering of another question, namely: does encephalitis infection confer immunity?

In regard to this problem science has not yet spoken its last word. In the epidemic anterior poliomyelitis, which resembles epidemic encephalitis in so many points as to make it justifiable to draw parallels, a rapidly acquired, practically persistent immunity, is the rule. (Wichmann). A reinfection with the virus of poliomyelitis is seen only very exceptionally in monkeys, as well as in man. Quite a few cases of reinfection in man, which seem fairly reliable, have been reported (Sheppard, Eckert, Sanz, E. W. Taylor)¹), but in all of these there was a more or less lengthened interval between the first and the second infection: 16, 6, 14, and 3 years, respectively.

Virus-destructive antibodies seem to be formed in the serum at a considerably later period in epidemic encephalitis than in poliomyelitis: Levaditti succeeded in destroying virus in vitro with a serum from a case of seventeen months' standing, while, for instance, serum from a case of three months' standing was ineffective.

Even though immunity is thus somewhat delayed in the case of encephalitic infection, we must at present suppose that immunity does occur, i. e. through the formation of antibodies in the serum. Kling, Davide &

¹) Journ. of nerv. & ment. dis. 1916 vol. 41 p. 207; cf. also Levaditti, loc. cit. p. 85.

Liljenkvist have made similar experiments as Levaditti & Harvier, with the serum from a case of more than a year's standing. Intracerebral inoculations on rabbits with encephalitis virus to which were added 2 parts of patient's serum, or 1 part of Berkefeld filtrate, only twice gave a reaction in twelve rabbits, whereas reaction was produced seven times by inoculation of cerebral substance to which was added normal serum.

Thus, the immunity seems to be very potent. As to how long it will persist nothing can be said at present, and, therefore, nothing definite either in regard to the possibility of reinfection.

Once more drawing an analogy with epidemic poliomyelitis, we must imagine a reinfection to be extremely exceptional, at any rate when the encephalitis infection has lasted more than about a year, or, inversely, when the infection is of so old a date that immunity can be supposed to have disappeared, such as it might possibly have done, for instance, in our Case 19.

Within the first year or so from the onset of an encephalitis, there is thus a possibility of a reinfection. The two (or more) attacks of a febrile nature, which are mentioned in several of our cases, might then perhaps be interpreted in this way. But, both as far as these infectious attacks are concerned, and in regard to the apparent "reinfection" in our Case 58, I think it far more natural to suppose a relapse. The analogies which can be drawn with poliomyelitis point in this direction, so does also the fact that encephalitis patients (as well as rabbits infected with the virus) — notwithstanding disappearance of the clinical symptoms extending over long periods — remain carriers of the virus, and, more especially, harbour a constantly active virus, as is reliably evidenced for instance by inoculation into rabbits of secretion from the naso-pharynx of these patients. Just as this virus may remain resistant to possible antibodies circulating in the blood, so also is the case undoubtedly in the central nervous system. In regard to poliomyelitis, — where

"relapses" may also be seen to occur occasionally in its first period (Wichmann), we know that the virus, in spite of the general immunity which, among other things, prevents experimental reinfection, — may keep out of the way of the destructive action of the antibodies, for instance in the spinal cord of monkeys (Leiner & Wissner). What has been supposed in regard to the micro-organism giving rise to poliomyelitis might therefore also obtain for that of epidemic encephalitis, namely that it, "tout comme les trypanosomes ou les spirilles, est capable de se vacciner contre les anticorps et se transformer en une variété anticorps-résistante, laquelle engendre la récurrence malgré la présence de substances bactéricides dans le sang" (C. Levaditti). On several occasions Netter, too, has drawn parallels between the behaviour of the encephalitis virus in the organism, and that of *spirochæta pallida*. More especially in regard to chronic encephalitis is there every reason to compare it with syphilis, at any rate to a certain extent, and especially as far as the chronic changes in the central nervous system are concerned. Also in the "metasyphilitic" affections, tabes, and general paresis, we find, on the one hand, immunity against infection and, on the other hand, the constantly active virus giving rise to relapses or, more often, to a chronic degenerative inflammatory process.

Finally, if we consider the histopathological picture, for instance that of our Case 58, this seems also to be far better explained by the recidivation theory, as evidencing one of the relapses which we know from clinical experience to be of such frequent occurrence in chronic encephalitis, as in fact to constitute a main feature in the general clinical picture of the disease. This seems far more natural than to suppose a reinfection, of which we only know, at any rate, that it must be of very rare occurrence.

PATHOPHYSIOLOGICAL MECHANISMS.

The elucidation of the pathophysiological mechanisms governing certain symptoms and syndromes in chronic epidemic encephalitis is, on account of certain facts, rendered somewhat difficult.

We have to deal with a disseminated (multilocular) affection of the central nervous system, involving functionally heterogenous sections of the same; and, on the other hand, it is an infectious disease, in regard to which the possible intervention of diffuse, toxic, perhaps extra-nervous factors, can never be excluded.

In spite of these difficulties we may venture to say that the pathophysiology of chronic epidemic encephalitis has its distinctive stamp in the relatively pronounced localisation of the morbid process to the basal ganglia and the brain-stem.

This obtains for instance in regard to the motor disturbances peculiar to encephalitis, namely parkinsonism and hyperkinesia. These are not due to an affection of the pyramidal tracts, but to involvement of the extra-pyramidal motor apparatus.

Fig. 85 gives a schematic representation of the more important components of this apparatus. Its one part, the cerebello-rubro-thalamo-cerebral pathway (2, 2, 2) is, as is well known, of great importance for the muscle tonus, the co-ordination and static function of the body. Its second part consists of the striatal system, the pathology and physiology of which we have learned a great deal about in quite recent years through the works of Anton, Bonhoeffer, Kleist, C. & O. Vogt, Kinier Wilson,

F. H. Lewy, Ramsey Hunt, Pierre Marie & Lhermitte, Trétiakoff, v. Stauffenberg, v. Economo, H. C. Hall, Stertz, Foerster, Bostroem, and others.

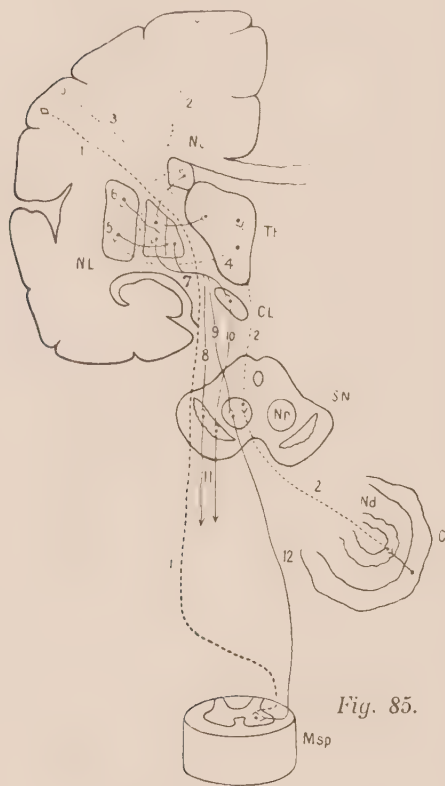


Fig. 85.

Fig. 85. — Diagram of the extrapyramidal system (modified after S. Kinier Wilson).

Th — optic thalamus. Nc — caudate nucleus. NL — lenticular nucleus, i. e. putamen (outer third) and pallidum (two inner thirds). CL — corpus Luysi. Nr. — red nucleus. SN — substantia nigra. C — cerebellum, with its dentate nucleus (Nd). Msp — spinal cord. 1 — pyramidal tract. 2 — cerebello-ponto-thalamo-frontal tract. 3 — thalamo-cortical fibres. 4 — thalamo-striatal fibres. 5, 6 — striopallidal fibres. 7 — pallido-fugal tract, to corpus Luysi, substantia nigra (8), the red nucleus (9). From the corpus Luysi fibres descend to the substantia nigra (10), from which fibres pass into the spinal cord (11). 12 — rubro-spinal tract.

This system consists chiefly of the striatal masses, the corpora striata (N. L., Nc) and the substriatal ganglion masses: the tuber cinereum, the corpus Luysii (N. L.), the substantia nigra (Sn), the nucleus ruber (Nr), the tegmental nuclei, and their connecting tracts. Phylogenetically and ontogenetically, as well as histologically and functionally, the corpus striatum may be divided into two parts: (1) the globus pallidus (the

"pallidum") and (2) putamen and the nucleus caudatus (the striatum proper, C. & O. Vogt), or, in Kapper's terms: the palæo- and neostriatum. The palæostriatum contains large (motor) cells exclusively, (of the Golgi's type I), the axis-cylinders of which form the striofugal tracts (7, 8, 9) leading to the substriatal ganglia. The neostriatum contains only a few of this type of cells, while mainly small and medium-sized cells with profuse dendrite ramification ("coupling cells") are found, the axis-cylinders of which form the strio-pallidal tracts (5—6).

The striatal apparatus is of decisive importance for the regulation of the muscular tonus, as it exerts an inhibitory influence on the tonigenic impulses from the cerebellum, most probably effectuated through the nucleus ruber (R. Bing) (and the thalamus?). This function seems to belong entirely to the palæostriatum (the pallidum) and the substantia nigra (Trétiakoff, Goldstein, Foix, Lhermitte, Spatz, Globus, F. H. Lewy, and others)¹.

Furthermore, the palæostriatum is a main centre for the primitive automatisms (C. & O. Vogt) which later in life are kept in check by the function of the neostriatum. This part of the brain thus becomes the superior centre of involuntary mimicry and gesticulation; of automatic associated movements and changes of position; of certain components in speech, deglutition, gait; of defensive and protective reflex movements, etc. In addition to this, however, the striatal system constitutes a "coupling (coordinating) apparatus" (F. H. Lewy) of extreme importance in voluntary movements, regulating the course of and the interplay between the various senso-motor processes (coordination and adaptation in strength and chronology of the individual impulses; the mutual gradation and equilibration of the same; the due succession and duration of the agonistic and antagonistic effect, etc., etc.).

A (destructive) affection of the palæostriatum gives rise to the "pallidal syndrome" (C. & O. Vogt)², i. e. "parkinsonism". hypertonia, (general) rigidity to the point of contracture; bradykinesia or akinesia; tremor; abolition of automatisms, etc. However, a (relatively) isolated involvement of substantia nigra may apparently give rise to similar symptoms (Brissaud, Trétiakoff, Foix, Lhermitte, Goldstein, Jacob, and others).

¹) According to Mirto, Trétiakoff, Hallervorden & Spatz, there is an intimate phylogenetic and histological correlation between these two striatal ganglia.

²) According to C. & O. Vogt only in case the affection is bilateral.

According to C. & O. Vogt an (isolated) involvement of the neostriatum produces the "striatal syndrome", i. e. a certain degree of akinesia and hypertonia and, in addition, and more especially, different forms of hyperkinesia, choreatic or athetoid movements, tremor, involuntary associated movements, spasmodic laughter and weeping, etc., etc., due to abolition of the inhibition on the substriatal ganglion masses. The observations made in Huntington's chorea of an involvement of the small and medium-sized ganglion cells in the neostriatum might serve to support Vogt's theory (Alzheimer, Pierre Marie & Lhermitte, Jelgersma, R. Hunt, F. H. Lewy, Jacob). Kinier Wilson, v. Economo, and others too, hold that an affection of the "lenticular nucleus" will give rise to hypertonia and tremor, alone, but not to athetosis or chorea. Moreover, it is quite certain that similar hyperkineses may arise in affections which are localised to other sections of the extrapyramidal system: the cerebellum, the crura, cerebelli ad pontem, the nucleus ruber, the hypothalamus, the frontal lobes, etc. It is perfectly justifiable, therefore, when several writers (Kinier Wilson, Lhermitte, F. H. Lewy) make their reservation in regard to immediately conceiving these motor disturbances as depending wholly upon an affection of the neostriatum.

As for epidemic encephalitis there is doubtless an extremely entangled integration of various nerve centres or tracts involved, the dominating features being sometimes symptoms of inhibition, and sometimes, rather, irritative phenomena, diaschisis factors undoubtedly also playing a rôle¹⁾.

While thus encephalitic parkinsonism must be supposed to be mainly dependent upon the localisation of the morbid process to the palæostriatum or to the locus niger, it is much more difficult to localise the hyperkinesia. F. H. Lewy suggests that, for instance the "pulsions", and certain of the tremors (for instance rotatory tremor of the head) found in paralysis agitans, might be due to a lesion of the cerebellum, more especially of the dentate nucleus. In our Case 60, presenting a

¹⁾ Other factors, too, may come in, e. g. the age of the patient (athetosis belongs predominantly to childhood); a certain "striatal predisposition", giving rise to more autonomic automatisms (cf. Case 36, 51), etc., etc.

severe motor unrest of the head (and the eyes), marked perivascularitic changes were found precisely in this locality. Also in Case 59 we found (chronic) vascular changes in the dentate nucleus; but, perivascularitic changes (and thromboses) were found more especially in the ponto-cerebellar tract. In Case 60 we had a degeneration of the right crus cerebelli ad pontem, and also a mild degeneration in the nucleus ruber. Again, our autopsies reveal severe pathological changes in the thalamus, sometimes amounting to softening (Case 60). It is well known that a lesion of the thalamus has been suggested by v. Monokow in cases of choreo-athetoid movements, which movements also, originally, formed part of the "thalamic syndrome" of Dejerine and Roussy¹).

Whether the myoclonias occupy a special position, as regards localisation and pathophysiology, is doubtful. On the basis of the special character of these motor disturbances, their restriction to one isolated or some few muscular groups, and of their being often accompanied by pains, sensory disorders, amyotrophias, of a radicular topography, hiccoughing attacks, etc., Mlle Lévy thinks it reasonable to infer a medullary or bulbo-protuberantial starting-point. She refers to a case of Foix', presenting rhythmical diaphragmatic jerks, in which the post-mortem examination showed that the encephalitic changes were restricted to the cervical part of the cord. Riley, v. Economo, and others, also hold to a predominant spinal genesis of the myoclonias. Stern is more reserved; he points out the rhythmical character of the twitches, which is not so readily understood on the supposition of a spinal origin, but better so on a mesencephalic one (Sicard). On the other hand, Stern thinks it reasonable to suppose a spinal origin for certain myofibrillary or myoclonic movements or for certain rhythmical twitches

¹) Roussy now seems to consider the hypercinetic disturbances of the syndrome as being of striatal origin. Klarfeld points out the almost constant involvement of the cerebello-rubro-thalamic tracts in acute choreatic encephalitis.

in parts of muscles, which he, too, has witnessed in muscular atrophies possibly of a spinal origin, or in muscles belonging to one and the same nuclear region. In an acute case he found very profuse infiltrations in the nuclei of the anterior horns (and the lateral columns). In our Case 60 there were perivascular infiltrations and destruction of the ganglion cells of the anterior horns, but, at the same time, severe alterations in the basal ganglia were also found. In Case 59 no distinct pathological changes could be found in the medulla oblongata.

Thus, at present, we are not able to say anything definite as to the starting-point of the myoclonic disturbances. It should be emphasised, however, that the more pronounced pathological changes are most frequently found in the brain; that the myoclonias often have a very diffuse distribution all over the body; that they are frequently intimately blended with other forms of muscular disorders of a certain striatal origin; and that they only rarely coincide with pronounced spinal symptoms, such as amyotrophies, localised disorders of sensibility, segmental or radicular pareses, or the like.

The speech disorders, the difficulties of mastication and deglutition, in chronic epidemic encephalitis are presumably of a striatal origin; inferior articulation centres for these functions are doubtless to be found in the region of the lenticular nucleus (Pierre Marie, Mingazzini, and others). As pathological changes are, however, usually to be found simultaneously in the bulbus, we cannot definitely exclude the possibility of a bulbar component in these encephalitic disorders. It must, however, be emphasised that true bulbar paretic symptoms are very rarely found in this affection, as has already been previously pointed out by Wilson in regard to progressive lenticular degeneration.

Spasmodic laughter and weeping were thought to be due to a lesion of the optic thalamus, by Nothnagel; and, it is true that direct pathological changes are frequently found in the thalamus in cases of chronic epi-

demic encephalitis. This "emotional incontinence" may possibly also, in some cases, be due to a deficiency of inhibitory influences from the affected corpus striatum.

The vegetative disorders frequently accompanying chronic epidemic encephalitis (p. 23) might, at a first glance, impress the observer as being of endocrinal origin. Definite alterations of the endocrine glands are, however, rarely found in chronic epidemic encephalitis (p. 291). An endocrinal involvement, if such were present in this disease, would also be strikingly "elective". Symptoms from the thyroid gland or the suprarenal capsules, for instance, are rarely found.

The symptoms belonging to the "hypophysis syndromes" such as adiposity (or cachexia), polyuria, polydipsia, glycosuria, changes in the sexual organs or in their functions¹⁾, constitute, in reality, the main features of vegetative disturbances in chronic epidemic encephalitis. A number of clinico-anatomical and experimental studies performed in recent years have, however, to a great extent unsettled our view as to these "hypophysis syndromes". A large number of experiments on animals²⁾ have pretty reliably established that in the basal grey matter of the brain, closely above the hypophysis, we have a series of vegetative (central sympathetic?) centres, situated in the tuber cinereum and the infundibulum, in the hypothalamus, which, if lesion occurs in any of them — although the pituitary body itself be untouched — may give rise to "hypophysis syndromes".

Aschner, and later, Bailey & Bremer, Camus & Roussy produced glycosuria by causing lesions to these centres³⁾.

¹⁾ I have not encountered any description of acromegalia, gigantism, or the like, in the literature on chronic epidemic encephalitis.

²⁾ Percival Bailey & Frédéric Bremer: *Arch. of intern. med.* 1921 vol. 28 p. 773; Jean Camus & Gustave Roussy: *Les syndromes hypophysaires*. *Rev. neur.* 1922 p. 662; F. H. Lewy: *Die Lehre v. Tonus u. Bewegung*. Berlin 1923 p. 361.

³⁾ Removal of the suprarenal capsules did not prevent the occurrence of the glycosuria.

Leschke, Houssaye, Camus & Roussy, Bailey & Bremer could produce polyuria and diabetes insipidus¹), also polydipsia, although less constantly. An adiposo-genital syndrome (polysarcia, testis atrophy, apathy, somnolence, and occasionally, diabetes insipidus) was produced experimentally both by Bailey & Bremer, and by Camus & Roussy. In a few of Bailey & Bremer's experiments, moreover, cachexia ("hypophyseopriva"), convulsions, and coma were induced.

It is thus rendered highly probable that polyuria as well as the adiposo-genital syndrome, and perhaps also glycosuria, are attributable to central vegetative (may be central sympathetic) disturbances. Camus & Roussy therefore suggest the term "syndromes infundibulo-tubériens" when these disorders are concerned²).

As a parallel to these experimental investigations we may mention Claude & Lhermitte's description of the infundibular syndrome resulting from an affection of the infundibular region, the pituitary body being unaffected; the symptoms are: narcoleptic crises; tachycardia, cardiac arrhythmia, extra-systole; polyuria and polydipsia³).

The histopathological changes found in chronic epidemic encephalitis are relatively frequently localised in the above mentioned cerebral areas, or, at any rate, in immediately adjacent parts. This is also an argument in favour of the probability of a central nervous genesis of the vegetative disturbances found in chronic epidemic encephalitis, such as is also supposed by v. Economo.

The cases of encephalitic pubertas præcox might lead our thoughts in the direction of lesions of the pineal

¹) This occurred also after previous extirpation of the hypophysis (which did not give rise to polyuria) as well as after denervation of the kidneys.

²) It seems that Roussy continues to consider acromegalia and gigantism as symptoms of lesions in the pituitary body.

³) Presse méd. 1917 p. 417. Compare: Claude & Schaeffer: Rev. neur. 1921 p. 25: Compression of the hypophysis alone, without infundibular symptoms.

body. Kn. Krabbe's survey¹⁾ of the importance of the pineal gland in regard to puberty, however, renders an endocrinal genesis very doubtful. In this connection, as well as in regard to the "hypophyseal" syndrome, one might just as well suggest an affection of cerebral nervous centres (v. Economo), the existence and localisation of which are, however, hypothetical so far.

Apart from these mesencephalic vegetative centres, we have, as is well known, the bulbar vegetative vagus nucleus ("sympathetic vagus nucleus", Marinesco) on the floor of the fourth ventricle. Brugsch, Dresel & Lewy, have in recent years examined the relations of this nucleus to the vegetative disturbances²⁾, and, by causing lesion to this area, they have produced changes in the sugar contents of the blood; glycosuria; changes in the excretion through the kidneys of water and sodium chloride, etc. In chronic epidemic encephalitis, where the medulla oblongata is not infrequently found to be the seat of perivascular infiltration or degeneration, we may therefore sometimes reckon with a bulbar origin of the vegetative disturbances.

In the striatal and more especially in the substriatal (subthalamie) region, we have also centres for the innervation of the vessels, for the functioning of the heart, for respiration, perspiration, pupillary movements (Karpus & Kreidl, Aschner, Garrelon & Launois, Bailey & Bremer, and several others). It is therefore reasonable to suppose that the disorders of these functions in chronic epidemic encephalitis may be, and usually are, of a central nervous origin, chiefly striatal or "substriatal", arising perhaps from a deficiency of the inhibitory influences exerted upon the vagus centre (Stern), or the like. As has already been mentioned (p. 71) a psychogenic (affectogenic) component might be supposed in the case of grotesque respiratory disturbances, and perhaps also

¹⁾ Endocrinology 1923 vol. VII p. 349.

²⁾ F. H. Lewy, loc. cit. p. 361, etc.

of certain types of tachycardia, congestive attacks, etc. Yet, this emotional instability, too, should in most cases undoubtedly be ascribed to an organic lesion (cf. below).

The possibility of a co-action of toxic factors must be considered in cases of disturbances of thermoregulation in chronic epidemic encephalitis. The peculiar "flat" temperature curve found in many encephalitic patients; the inversion of the temperature rhythm (Sicard, Misch); observations made in other instances of "brain fever"¹⁾, will, in many cases, tempt the observer to suppose that the central nervous mechanisms governing these functions are affected through a direct involvement of the heat regulating centres which, in a number of animal experiments, have been demonstrated to have their site in the corpus striatum and especially in the tubero-infundibular and hypothalamic region (Aronsohn & Sachs, Richet, Baginsky & Lehmann, Girard, Loeb, Isenschmidt & Krehl & Schnitzler, Ott, Leschke, Barbour, Hall White, Bailey & Bremer).

In the mid-brain we have thus a considerable number of vegetative centres which are of fundamental importance to blood-circulation, respiration, and the entire chemism of the body. It seems, therefore, reasonable to conclude that lesions in this cerebral region, by causing disturbances of various kinds and in various combinations to these centres, may, generally, give rise to sleep disorders, either persistent or episodic, such as are found in epidemic encephalitis, in the acute stage as well as in the chronic form of the disease.

At any rate, I find it difficult to understand these sleep disturbances, — in the first place the "lethargy" —, as being due to the individual factors set up by various authors to account for them, namely: "increased intracranial pressure" (Buzzard), which is utterly hypothetical; "interruption of the sensory impulses to the thalamus" (Gayet, Trömmer), of which the same may be said; dis-

¹⁾ D. Hinsch: *Zeitschr. f. ges. Neur. u. Psych.* 1920 Bd. 54 p. 303; Misch: *ibid.* 1921 Bd. 66 p. 59.

turbances of the muscle tonus (Marinesco, and, to some extent also Stern); hormonal processes (Salmon, Mingazini); pareses of the eye muscles (v. Economo). The last mentioned factors may possibly be of some importance as contributory agents in bringing about lethargy, in my opinion, however, only when working on the basis of a previously evoked general change of biotonus through a more diffuse action on the mentioned vegetative centres.

At any rate, one should be a little reserved in speaking of a "sleep centre" (having its seat in the neighbourhood of the eye muscle nuclei; v. Economo).

Neither are the patho-physiological mechanisms governing the psychic and nervous disturbances found in chronic epidemic encephalitis very easily seen through.

The more neurastheniform disturbances are, in the main, identical to those found as sequels to other chronic or acute infectious diseases, and should perhaps be considered as manifestations of a more general impairment ("fatigue") of the nervous system. A similar origin might be imagined for the more permanent unbalancing of the patient's emotions. The excitability, the emotional erethism, is a well known feature of "nervous fatigue" in all its forms. As regards chronic encephalitis, however, owing to the pronounced pathological changes found in the basal ganglia, one is tempted to infer a more "focal" component. We might, here, draw an analogy for instance with certain infantile brain affections, such as Little's disease, double congenital athetosis, etc., in which the emotionalism (amounting to spasmodic crying and laughter), is a very dominant factor, and, with regard to which there is an increasing tendency in recent research work to seek the main seat of the affection in the basal cerebral ganglia. Further reference to this subject will be made later.

The cerebral cortex is undoubtedly not wholly unaffected in chronic epidemic encephalitis. Certain of the psychotic and general nervous symptoms might therefore be thought to be dependent upon cortical lesions. In

the majority of cases, however, any severe cortical affection is hardly likely, among other things because it is only quite exceptionally that we have a true dementia, such as is to be found in the paralytic or senile cortical affections, for instance.

The psychotic disturbances found in children frequently bear a strong resemblance to the psychic unbalancing inherent to adolescence. We might perhaps here imagine a pathophysiological co-efficient in an action on consciousness on the part of the precocious puberty processes, which are not infrequently found to occur parallel with the psychic changes, in the first place with the "hyperkinetic" disturbances.

As for the bradyphrenia, we cannot help being struck by the remarkable resemblance between, and coincidence of, the physical and psychic rigidity. Several authors, also, conceive the psychic symptoms of bradyphrenia as chiefly dependent upon a lesion of the basal motor centres.

A certain connection seems here unquestionable. Bostroem¹⁾ thus points to the fact that the normally automatic coordinated and associated movements must, in a patient suffering from encephalitic parkinsonism, be replaced by voluntary movements (if the patient does not prefer to keep totally inactive)²⁾. The patient is thus compelled to pay attention to the individual partial components in the movements, which means an abnormal strain on his attention, with a chiefly "motor focussing", hence, a narrowing of the attention field, an intense and more rapidly ensuing fatigue of the attention which, as is quite understandable, will gradually tempt the patient to a certain "motor lassitude".

This predominantly "motor focussing" of attention may no doubt give rise to a certain degree of indifference to external impressions, a certain "apathy" towards the surrounding world, and, to a certain extent, a nar-

¹⁾ Zeitschr. f. ges. Neur. u. Psych. 1922 Bd. 76. p. 444.

²⁾ cf. the patient mentioned on p. 51 and 215.

rowing of the patient's process of thinking and stream of ideas.

Claparède and Naville¹⁾ tested the faculty of reaction of such patients, by subjecting them to tests demanding some reflection, concentration of attention, and combining faculty. The reactions were considerably retarded.

To account for this slow thinking and the monotonous range of ideas in these patients, I might further imagine, as a contributory factor, disturbances of the verbal-motor component of their complexes of ideas. Although to a varying extent in different individuals, "inward speech" (endophasia, G. Ballet), the "kinesthetic" speech components (from tongue, lips, throat, etc.) undoubtedly play a rather important rôle in all people, and the more so, the more the person concerned is of the "motor type" of thinking (Charcot). A reduction, or a retarded evocation of these "subcortically (striatally?) elicited verbal-kinesthetic sensations, of this motor component in the "word picture", is hardly without significance to the course of association of ideas, in so far as the more inconscient, "automatic" evocation of associations thus becomes inhibited or abolished. Anyone who has had the opportunity of talking a foreign language, will know how much less of a strain to his course of thinking it is "when the words are born on his lips", when "one word brings on the next one", that is to say when speech is conveyed partly by purely motor kinesthetic components, and the process of thinking s. s. need only to be interfered with once in a while, just to give the "cue". The more unfamiliar one is with the verbal-motor mechanism of a foreign language, the more noticeable becomes the limitation, a monotony amounting to stereotypy, of one's course of thinking.²⁾

¹⁾ L'Encéphale 1922 p. 424.

²⁾ This, of course, applies only in case one "thinks" in the foreign language. Otherwise, the train of thinking (in the native tongue) goes on independent of the paucity of the verbal-motor mechanisms. As far as the non-polyglottic encephalitic patients are concerned, however, this factor does not enter at all.

The appearance of tachyphemia and pallilalia might perhaps be accounted for by supposing a more positive hyperkinetic disturbance, a striatal irritation (Logre)¹. And, again, similar primary irritative conditions extending from the corpus striatum to the cortex cerebri might be conceived also in the event of the psychic erethic states in children, polypragmasia, motor restlessness, and the like

v. Economo sees in the reduction or abolition of these striatal (extrapsychic) motor components the essential cause of the "lack of impulses" (Meyer-Gross & Steiner)², or akinesia, frequently so evident in encephalitic parkinsonism. v. Economo is perhaps a little incautious in attributing a primary disturbance of a psychic function, such as "volition", to a localised affection outside the cerebral cortex. It is, however, highly probably that, in this case, as well as in the case of speech and thinking, there is an "integration", a co-operation of two parallel functions, the one cortical, the other subcortical. It is scarcely quite accidental that a person who shows habitual motor torpor, is frequently also intellectually torpid.

An essential causative factor, apart from those pointed out before, of the reduced or abolished "mobility" found in these patients, is, doubtless, "the lack of feeling" of which so many of them complain. According to what I have gathered by talking with my patients is is not a question of abolition of the primary emotional tone of impressions or ideas, nor of paradoxical feelings, the impressions being predominantly attended by unpleasantness, for instance. What these patients complain of, and often feel very painfully, just because their primary (cerebral) emotional tone is intact and quite adequate,

¹) Congr s de Quimper. Rev. neur. 1922.

²) Encephalitis lethargica in der Selbstbeobachtung. Zeitschr. f. d. ges. Neur. u. Psych. 1921 Bd. 73 p. 283.

is, that the "emotional resonance" fails them. Their emotional condition is, in this respect, very similar to that of patients suffering from melancholia.

However one looks upon James-Lange's theory on emotions, generally, it is now universally recognised that the true "emotional resonance", the affective process, *s. s.*, should not be considered as a purely cerebral one, but that a multitude of elements go to constitute the affective states, elements constituted of sensations due to all the somatic changes brought about by the primary cerebral ideo-emotional complex. This widespread somatic integration is absent or markedly reduced in patients suffering from encephalitic parkinsonism.

This difficulty of emotional response (Hauptmann), this "lack of feeling", as it is usually termed by the patients, seems to me to be most readily understandable when attributed to disturbances of function of the various basal centres for vegetative life, which have been mentioned above, and through which the "transmission" of the primary cerebral process as an "emotional reaction", no doubt, takes place. It is the hypofunction (or afunction?) of these centres, of which the patient becomes conscious; it is the same which gives the stamp of slowness and paucity to his process of thinking, of sluggishness and want of initiative to his volition, on the ground that the emotions are extremely important "motor factors" of our psychic life.

And, inversely, a hyperfunction of these centres, or a lowering of their threshold of excitability, might be supposed to give rise to the emotional erethism presented by other of the clinical pictures of chronic encephalitis, which has been mentioned on several occasions in this work.

Finally, this severe disturbance of the mode of function of the "centres of emotion", as regards excitability and character of responding "primitive automatisms", tends to explain the semiological resemblance between certain

chronic-encephalitic symptoms and certain of the kinetic manifestations of hysteria and dementia præcox (catatonia).

The hysterical or psychogenic manifestations can be understood as pathologically exaggerated or caricatured, complete or dissociated emotional reactions, such as it was already held by Briquet and also has been more recently advanced, for instance, by Kraepelin, Mott, C. & O. Vogt, Roussy & Lhermitte, and several others. Hysteria, in its "crises" or other "hyperkineses", will thus make use of our primitive "expression mechanisms", i. e. of just those motor and vegetative primary functions which are affected also in chronic encephalitis, hysteria having, on the whole, its vasomotor, vegetative and, therefore, to a certain extent also its psychic instability, in common with chronic epidemic encephalitis¹⁾.

Again, as has been said before, a similar psychogenic, emotional origin (Bleuler) may be supposed in regard to several, perhaps the majority of the individual catatonic symptoms in dementia præcox, these psychic mechanisms working in an organically changed brain. Many of the bizarre postures and manners, stereotypies, rhythmic movements, etc., found in catatonia, evidence by their character alone, even at an advanced stage of the disease, their psychogenic origin, being understandable as expression manifestations, stiffened, automatised, dissociated movements, representing the patient's delusions, hallucinations, emotional rigidity or emotional ambivalence, such as is also frequently the case with the patient's negativism.

No doubt, the autistic, catatonic patient, with his clumsy and sluggish movements, his catalepsy, his automatisms, etc., may, like the stuporous one, recall the picture of the motor viscosity of parkinsonism. Yet, one need only to follow these cases some little time to learn the most astonishing way in which these motor disturbances will

¹⁾ Compare C. & O. Vogt: *Pathol. Veränd. d. Striatum*. Sitz. Ber. d. Heidelberger Akademie 1919.

suddenly disappear, spontaneously, on extrinsic stimuli, etc., giving way, for instance, to a quite vehement catatonic excitement, with excessive motor unrest, etc. We may even come across patients who have, for years, been lying in a most complete stuporous state, and who will suddenly "wake up", without any impairment, at all, of their motor functions, not infrequently giving a most reasonable explanation of their motor inactivity (delusions, imperative hallucinations, and the like). Thus, notwithstanding the most interesting findings of Laig-nel-Lavastine & Bertrand of "plaques cyto-graisseuses" in the basal ganglia of dementia præcox patients, I should not be inclined, generally, at least, to admit a striatal origin of the motor troubles met with in this disease.

Here, as in the case of hysteria, there is a semiological resemblance, because the sick consciousness works by means of the same primitive nervous functions as in chronic encephalitis. Hence it does not follow, however that there should be any nosological or etiological connection between these diseases, no more than between hysteria and catatonia.

COURSE AND PROGNOSIS.

Vous voyez comment il est malaisé de
porter un pronostic dans cette maladie :
on ne sait quand elle finira et l'on ne sait
pas toujours quand elle est finie.

ACHARD.

That we are still rather groping in uncertainty in regard to the course and prognosis of this disease is not only attributable to the short space of years which has elapsed since epidemic encephalitis began to ravage the world. The very nature of the morbid process, the capricious way of its quietening down for a period to flash up again, however, seems to mock any attempt at prognosis. "Surprising" seems to be a most adequate epithet for this disease.

At present, we can only say that in cases of chronic epidemic encephalitis the prognosis is always dubious. And, the more so perhaps, the more "insidious" or gradually chronic the course of the disease has tended to be from the onset.

In point of principle, we must suppose that chronic epidemic encephalitis is curable, in as much as the morbid process may come to a stop, leaving or not leaving defect symptoms. Unfortunately, however, a favourable issue seems to be exceptional. Of my cases, I should not reckon with more than a few instances of this kind. Here, again, we shall have to await further experiences before we are in a position to say anything definite. Considering the tendency to a protracted course, shown by the majority of cases of chronic epidemic encephalitis, it can by no means be taken for granted that none of the patients who are at present under observation, will be cured; perhaps, however, only in the

course of years; or, at any rate, it is possible that some cases may become "stationary".

Occasionally, again, even in rather severe cases (such as Case 41) we may be surprised by witnessing a recovery which seems to become permanent, and thus not only to be one of those remissions which, in this disease, so frequently disappoint both the physician and the patient.

On the other hand, we have in my material cases which, from the very onset, are stamped by a cheerless tendency to progressiveness, the general health of the patient being affected at an early stage (cachexia, etc.), so that a fatal issue is soon suspected.

In the majority of cases, however, any attempt at prognosis is foiled by the erratic course of these nervous diseases.

According to my personal experience, the uncertainty of prognosis is almost equal in all the various clinical types. It has been supposed that parkinsonism (or at any rate certain forms of it, for instance those without tremor), should have a relatively more favourable prognosis in young people. Sicard, Stern, and others too, failed to state such a fact. Among my parkinsonian patients, a few showed a pronounced tendency to improvement, some young people, and the man mentioned as Case 7, who is now forty years of age. But in other cases of parkinsonism, that is to say in the majority, the affection has been progressive, or at any rate, stationary, up till the present time, i. e. through several years.

Certain cases of the hyperkinetic types, for instance myoclonias, should, according to Naville, possess a relatively more favourable prognosis; whereas Mlle Lévy, Krebs, and others, regard just these forms of encephalitis as being extremely tenacious. v. Economo, and Sicard say the same of the choreo-athetoid types, which is also in keeping with our Case 46, and with our Case 47, of the torsion spasm type.

Altogether, my material has yielded the definite impression that, at any rate, cases which present marked extrapyramidal syndromes belong to the most long-standing category, and have always a dubious prognosis. Stern's experiences point in the same direction; more especially in regard to those cases in which the extrapyramidal syndrome sets in late in the disease, following upon a quiet interval. Bing has made the same observation as regards parkinsonism¹). It is quite likely that, in the event of a well marked extrapyramidal syndrome, such as for instance a parkinsonism, a general chorea or myoclonia, there is chiefly a question of degeneration processes in the central nervous system, that is to say morbid changes which are likely to be less capable of restitution than, for instance, the exudative-infiltrative processes.

The cases of children, showing predominant psychotic symptoms (change of character, and the like), seem also to be extremely tenacious, which is of great importance as regards the question of treatment and accommodation of such children.

Among the "intermediary" types, some are just characterised by their intermittent-paroxysmal course; thus for instance, the encephalitic epilepsy, the apoplectiform type, etc. As a matter of course, there is no possibility of giving a prognosis in these cases. I have formed the impression, however, that in some few cases, a true cure of the disease has actually taken place, it being not only a question of an intermission (Case 55).

The findings in the cerebrospinal fluid, the temperature curve, etc., scarcely give us any prognostic clues. Nor do I think that any of the individual symptoms afford such clues.

As to the influence of the patient's age on the course and issue of a chronic epidemic encephalitis, I do not think there is any striking difference. It may be surmised,

¹) Schweiz. med. Wochenschr. 1922 No. 6.

however, that the prognosis, to some extent, becomes still less favourable when there is marked senility, or arteriosclerosis.

To sum up, therefore, we may say that no reliable forecast can be given in the concrete case, the prognosis being mostly guess-work. The disease may have a course ending in perfect recovery; or, it may become stationary. It may be progressive, either gradually, with or without the appearance of new nervous symptoms; or the course may be remittent-exacerbating or intermittent-paroxysmal. It may end in death either through a protracted, cachectic state, or by a sudden aggravation (relapse) as in some of our cases.

Future investigations, it is to be hoped, will enable us more reliably to forecast the different possibilities.

TREATMENT.

Unfortunately, this chapter can, as regards chronic epidemic encephalitis, be made a very brief one: we are, as yet, in the experimental stage, only.

We have no therapy which aims directly at overcoming the pathogenic noxa. Opinions differ greatly as to the effect of a serum therapy, employing convalescents' serum. Netter, Lévy & Sicard, and several others, saw no effect at all. Stern, and Grünwald, seem to be better satisfied. Principally in acute cases, but also, according to Stern, in chronic cases, these authors appear to have seen some result of a serum treatment. Stern applies intramuscular injections of 40—50 ccm of convalescent's serum, "die beliebig oft wiederholt werden können". He emphasises that the serum should, of course, be obtained from true convalescents, which, according to what has been said in this work, it may in fact be difficult to ascertain. Moreover, Stern does not think it safe to assert that there is a specific action of the serum and not only a non-specific action of protein substances.

An "autohematotherapy" has been recommended by Mouriguand, Bourges & Marcandier, the results being however negative, and, also, intravenous injections of the patient's own cerebrospinal fluid (Piticariu), a treatment which Souques & Mourgain tried with ten patients, without any definite effect¹⁾.

Nor have any results been obtained by attempts at treatment with subcutaneous injection of an aqueous extract from the cerebral peduncles or the corpus striatum (Sicard & Paraf). The same may be said of the "artificial

¹⁾ Revue neur. 1922 p. 1356.

fever treatment" set up either through fixation abscesses (Netter), or through an inoculation with malaria (Nonne), or injections with nucleic acid sodium, etc.

Antibacterial treatment with iodine has also been tried: intravenous injections of Pregel's solution in rapidly increasing doses, up to 100 ccm of the solution, applied intravenously three times a week, amounting to a total of 1—1 1/2 l. (v. Economo). Others have tried urotropine (uroformin), the favourable effect of which has been pointed out by Froment & Generevois. Silver salvarsan, neosalvarsan, electrargol, cacodylate of sodium (Lhermitte & Sicard, and others), have likewise been used in the numerous attempts which have been made to defeat this disease; usually, however, only with transient results.

In my own department, having been disappointed in all the above-mentioned remedies, we have, for a rather long period, worked with the argotropine preparation recommended by Marburg¹⁾; it is a combination of 1 % colloidal silver and 20 % hexamethylenetetramine. It is administered intravenously, in doses of 5 ccm, i. e. 1 ampule. At first we did not venture to follow the original directions: 1 ampule daily, but reduced the dose to 6 to 9 ampules in all, given at 2 to 4 days' interval. The immediate reaction was in our cases slight, a little fever following on the first one or two injections, while, otherwise, there was no unfavourable reaction. We have now proceeded to use a series of 10 injections, one every second day, and then an interval of 4 to 5 days, if another series is to be given. In some few cases, finally, we have followed the original directions of Marburg, viz. an every day injection, without unfavourable results.

As for the various clinical types, I think I have even observed a markedly good effect from this remedy, such as for instance in the Cases 7, 32, 45, and also in a young patient of the Parkinsonian type, who has not been included in the present material.

¹⁾ Neurol. Zentralbl. 1921 p. 90.

A purely palliative therapy is, of course, of the greatest value in so painful an illness as chronic epidemic encephalitis frequently is.

In some cases of hyperkinesia, more especially the myoclonic or choreatic types, for instance in Case 41, I saw a strikingly good effect from a combined treatment with luminal (0,05—0,10) and phenacetin (0,25—0,50). To alleviate the violent tremor or painful rigidity in parkinsonism we must often have recourse to hyocine (Babinsky, Souques, and others), cicutine (Pierre Marie, & Boutier), tincture of arnica (Guillain), etc.

And, in addition to this, in parkinsonism, a treatment with hot baths, gentle massage, continuous mild gymnastics, and the like, is to be recommended.

The agrypnia frequently shows a desperate resistance to our narcotics so that we have to give very large doses and often change the remedies.

In the case of certain psychotic disturbances, erethic exaltation in children, general nervous disturbances in children as well as in adults, fits of anxiety, emotional hyperexcitability, tachycardia, respiratory tics, etc., a treatment with bromides, perhaps in combination with small doses of codein, is to be recommended. Whereas I would regard it a mistake to commence a treatment with morphia or opium in these patients whose affection is, in the majority of cases, of very long standing. It is a different matter, of course, in the hopeless and terminal stages of the disease.

In cases of excessive emaciation or cachexia a roborant treatment of course is indicated, for instance with cacodylate. Whether a specific hormone treatment should be tried in the case of certain of the syndromes which have a dyscrinal aspect, would seem rather doubtful in the light of the foregoing discussions on these matters. Yet, in a woman of 32 years, manifesting a slight encephalitic parkinsonism, a marked adiposity and oliguria, a thyreodine treatment showed a remarkable effect upon the basal metabolism. This, being tested twice

before the treatment, in the Standard metabolism apparatus of Marie Krogh, revealed a deficit of 30 %. Then, for some six weeks, the patient was given a tabloid of thyreodine (containing 200 hormon units), thrice daily. The Standard metabolism being again twice tested, now showed a deficit of 5 %, only, the patient having lost about 2 kgs. in weight.

Finally, chronic epidemic encephalitis has, also, a psychotherapy which, of course, principally, comes into consideration in regard to the psychic disturbances found in children and quite young individuals. In addition to a medical treatment, if such is needed in these patients, an educational treatment will also be necessary, a course of instruction which aims at redressing the intellectual disturbances (the hypervigilant, rapidly tired attention, etc.); a disciplinary training as regards the characterologic and moral changes. The child will often have to be removed, not only from school, but also from its home; children of well-to-do parents may be accommodated for in private educational homes under the supervision of a physician, or the like. In many cases the child or youth will have to be placed under the public care in homes for psychopaths or in special hospitals for the mentally defective, if such are available. An ordinary department for mental diseases, among adults, is hardly applicable in such cases. And still less so are the ordinary public educational institutions, for even if these minor patients are up to a certain point "criminals", they are nevertheless diseased.

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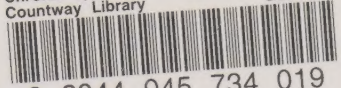
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